A PROSPECTIVE STUDY OF CORRELATION BETWEEN SERUM URIC ACID AND DYSLIPIDEMIA IN ESSENTIAL HYPERTENSION

Dissertation submitted to

THE TAMILNADU DR.M.G.R MEDICAL UNIVERSITY

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In partial fulfilment for the Degree of

DOCTOR OF MEDICINE

BRANCH I –M.D.,(General Medicine)

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DEPARTMENT OF MEDICINE

TIRUNELVELI MEDICAL COLLEGE

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TAMILNADU

CERTIFICATE

This is to certify that the Dissertation entitled "**A PROSPECTIVE STUDY OF CORRELATION BETWEEN SERUM URIC ACID AND DYSLIPIDEMIA IN ESSENTIAL HYPERTENSION"** is a bonafide original work of Dr.R.KUMAR **,** in partial fulfilment of the requirement for M.D., BRANCH I General Medicine Examination of the The Tamilnadu Dr.M.G.R. Medical university, Chennai to be held in April 2015.

The bonafide work is carried out by him under my guidance and supervision. This dissertation partially or fully has not been submitted for any other degree or diploma of this university or other.

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CERTIFICATE OF REGISTRATION & APPROVAL OF THE TIREC REF NO: 356/GM/2013/29.0[illegible]13

PROTOCOL TITLE: A Prospective Study of Correlation between Serum Uric Acid and Dyslipidemia in Essential Hypertension

NAME OF PRINCIPAL INVESTIGATOR: Dr.R.Kumar

DESIGNATION OF PRINCIPAL INVESTIGATOR: Post Graduate Resident

DEPARTMENT & INSTITUTION: Department of General Medicine, Tirunelveli Medical College

Dear Dr Dr.R.Kumar, *the Tirunelveli Medical College Institutional Ethics Committee (TIREC) reviewed and discussed your application during the IEC meeting held on* 29.0[illegible]2013.

THE FOLLOWING DOCUMENTS WERE REVIEWED AND APPROVED

1.	TIREC Application Form	☑
2.	Study Protocol	☑
3.	Department Research Committee Approval	☑
4.	Patient Information Document and Consent Form in English and Vernacular Language	☑
5.	Investigator's Brochure	☑
6.	Proposed Methods for Patient Accrual Proposed	☑
7.	Curriculum Vitae of the Principal Investigator	☑
8.	Insurance /Compensation Policy	☐
9.	Investigator's Agreement with Sponsor	☐
10.	Investigator's Undertaking	☑
11.	DCGI/DGFT approval	☐
12.	Clinical Trial Agreement (CTA)	☐
13.	Memorandum of Understanding (MOU)/Material Transfer Agreement (MTA)	☑
14.	Clinical Trials Registry-India (CTRI) Registration	☐

THE PROTOCOL IS APPROVED IN ITS PRESENTED FORM ON THE FOLLOWING CONDITIONS

1. The approval is valid for a period of 2 year/s or duration of project whichever is later
2. The date of commencement of study should be informed
3. A written request should be submitted 3weeks before for renewal / extension of the validity
4. An annual status report should be submitted.
5. The TIREC will monitor the study
6. At the time of PI's retirement/leaving the institute, the study responsibility should be transferred to a person cleared by HOD
7. The PI should report to TIREC within 7 days of the occurrence of the SAE. If the SAE is Death, the Bioethics Cell should receive the SAE reporting form within 24 hours of the occurrence.
8. In the events of any protocol amendments, TIREC must be informed and the amendments should be highlighted in clear terms as follows:
   a. The exact alteration/amendment should be specified and indicated where the amendment occurred in the original project. (Page no. Clause no. etc.)
   b. The PI must comment how proposed amendment will affect the ongoing trial. Alteration in the budgetary status, staff requirement should be clearly indicated and the revised budget form should be submitted.
   c. If the amendments require a change in the consent form, the copy of revised Consent Form should be submitted to Ethics Committee for approval. If the amendment demands a re-look at the toxicity or side effects to patients, the same should be documented.
   d. If there are any amendments in the trial design, these must be incorporated in the protocol, and other study documents. These revised documents should be submitted for approval of the IEC, only then can they be implemented.
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   f. The amendment is unlikely to be approved by the IEC unless all the above information is provided.
   g. Any deviation/violation/waiver in the protocol must be informed

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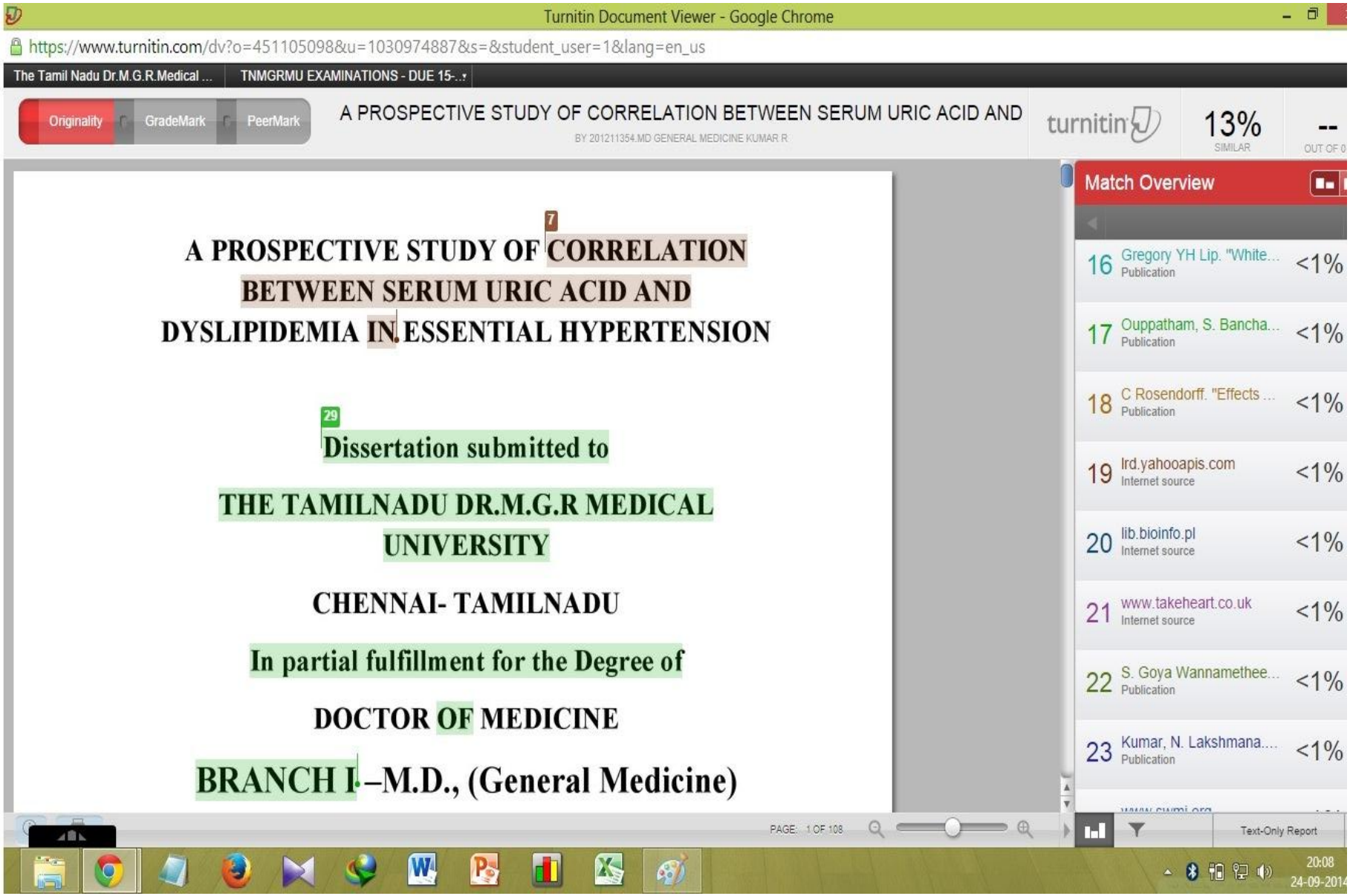
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DECLARATION

I**, Dr.R.KUMAR**, solemnly declare that, I carried out this work on **"A PROSPECTIVE STUDY OF CORRELATION BETWEEN SERUM URIC ACID AND DYSLIPIDEMIA IN ESSENTIAL HYPERTENSION"** at Department of General Medicine, Tirunelveli Medical College and Hospital during the period of August 2013 and August 2014.

I also declare that this bonafide work or a part of this work was not submitted by me or any others for any award, degree, diploma to any university, found either in India or abroad.

This is submitted to The Tamilnadu Dr.M.G.R. Medical University, Chennai, in partial fulfilment of the rules and regulations for the MD Degree Branch I General Medicine Examination, to be held on April 2015.

Place : TIRUNELVELI

DR.R.KUMAR ,

POST GRADUATE,

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THANKS TO THE IMMORTAL POWER WHO HAS BESTOWED UTMOST KINDNESS ON ME

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Last but not the least, on the recollection of so many and great favours and blessings, I now, with a high sense of gratitude, presume to offer up my sincere thanks to the God Almighty, the Creator and Preserver.

CONTENTS

A PROSPECTIVE STUDY OF CORRELATION BETWEEN SERUM URIC ACID AND DYSLIPEDEMIA IN ESSENTIAL HYPERTENSION

ABSTRACT

BACK GROUND:

The association of serum uric acid with various cardiovascular risk factors have led to the debate that whether serum uric acid can be an independent risk factor in essential hypertension. Hence we carry out a study to examine the possibility of hyperuricemia in hypertension, to see if there is a relationship between the serum uric acid levels and hypertension. Hypertriglyceridemia, hypercholesterolemia, raised LDL, raised VLDL and a decreased HDL is seen in Essential hypertensives. So we examine the possibility of occurrence of dyslipedemia with respect to essential hypertension, in comparison with normotensive. Uric acid levels tend to rise with individual rise in any one of lipid parameter in hypertensive cases, in comparison to normotensives.so we evaluate the correlation of serum uric acid and dyslipedemia in essential hypertensive in comparison to normotensive. As the age increases in hypertensives, dyslipidaemia and hyperuricemia increase together, indicating uric acid as a risk factor for hypertension and its complication .The complications of hypertension like CCF, heart failure occur more due to endothelial dysfunction due to dyslipedemia and raised serum uric acid. Thus, the predilection of correlation between serum uric acid and dyslipedemia in essential hypertension will help in better management of essential hypertension and thereby preventing associated morbidities and mortalities.

AIMS OF THE STUDY:

1. To measure the fasting serum uric acid levels in essential hypertensive individuals aged between 35 to 65 years and in healthy individuals aged between 35 to 65 years.

2. To measure the fasting serum levels of lipid parameters triglycerides, total cholesterol, LDL, VLDL and HDL in essential hypertensive individuals and healthy individuals aged between 35 to 65 years

3. To analyse the possibility of correlation existing between fasting serum uric acid levels and fasting serum lipid parameters.

METHODS: A Case control study consisting of 30 controls, who are healthy individuals in the age group of 35 to 65 years, with blood pressure of <140/90 mmhg and 30 hypertensive cases who are individuals in the age group of 35 to 65 years with blood pressure of >140/90mmhg is undertaken to study the relationship between serum uric acid and lipid parameters in essential hypertension in comparison to normotensive. The current study is done In Tiruneveli Medical College, Department of Medicine from our inpatient and outpatient departments from August 2013 to August 2014. Diabetes mellitus, ischemic heart disease, renal disease, jaundice, chronic liver disease, familial hyperlipidemia, patients on lipid lowering drugs, smoking, alcoholics, obese individuals and gout patients are excluded from the study population by history and physical examination. All the study population are undergone physical examination and their fasting serum uric acid and serum lipid profile taken for analysis. The information collected regarding all the selected cases were recorded in a Master Chart. The range, frequencies, percentages, means, standard deviations, chi square, 't' value and 'p' values were calculated. Student's 't' test was used to test the significance of difference between quantitative variables .Yate's and Fisher's chi square tests for qualitative variables. A 'p' value less than 0.05 is taken to denote significant relationship.

RESULTS: Blood pressure elevation is observed as the age group increases. As age increases, a rise in blood pressure elevation is observed. The level of blood pressure rise is observed more in 55-65 year age group. Also more number of hypertensives are observed in 55-65 age group. An elevated level of triglycerides, LDL, VLDL and decreased level of HDL is observed more in hypertensive group (P <0.001significant). About 24 out of 30 cases in the hypertensive group has observed to have dyslipidemia ,either as total increase in all lipid parameters or increase in any one of the lipid parameter ,excluding HDL. In control population only few of the individuals have dyslipidemia, most of the control population do not have any lipid abnormality. Only 4 of 30 have increased triglycerides and 2 of them have increased cholesterol levels. So, about 80% of hypertensive population have dyslipidemia. In control population, only 20% have dyslipidemia and they too have only increased triglyceride levels. Also the rise in lipid parameters is more with age group, more seen in 55-65 years age group and the elevation also increases with increase in blood pressure. Uric acid elevation is seen in most of the individuals in hypertensive group (P <0.0001- significant). About 25 of 30 people have elevation of serum uric acid and its elevation is directly proportional to rise in blood pressure. Uric

acid level is not elevated in control group. The dyslipidemia is associated with elevation of serum uric acid in hypertensive group, where as in control group dyslipedemia is not associated with elevation of serum uric acid.

CONCLUSION: Dyslipidemia is seen in essential hypertensives. Elevation of triglycerides, rise in total cholesterol, raised LDL and raised VLDL and a decrease in HDL is observed in essential hypertensives. Elevation of serum uric acid level is seen in essential hypertensives. Both dyslipidaemia and hyperuricemia observed to be elevated with increase in age in essential hypertensives. In normotensives, few have elevated triglyceride levels and elevated total cholesterol levels. Though hypertriglyceridemia increases as age increases, it is not associated with hyperuricemia. This concludes that dyslipidemia is correlated to hyperuricemia in essential hypertensives and not in normotensives.

KEY WORDS: serum uric acid, dyslipedemia, essential hypertension, correlation,

INTRODUCTION

Hypertension is one among the most vital non communicable diseases contributing to global burden of morbidity and mortality and one of the vital cause leading on to death. Hypertension has been associated with increased incidence of cardiovascular pathology, which includes coronary artery heart disease, heart failure, ischemic and haemorrhagic stroke, renal disease, and peripheral arterial disease. It has been seem to be linked with cardiovascular risk factors, and so the risk amount increases with the total weight of risk factors.

Even though it is present worldwide, the major toll occurs in the developing nations rather than developed nations due to unawareness and inadequate treatment[1]. Proper educational strategies will help to manage the epidemics of hypertension[2].

Even treatment of hypertension seems to reduce the risks of cardiovascular and renal pathology, majority of the hypertensive group are not treated sufficiently, due to unawareness of the problem[4].Among hypertensive, renal disease is an important complication especially with more severe Hypertension[5].

The Asia Pacific cohort studies collaboration clearly demonstrated the log linear relationship of blood pressure with ischemic & haemorrhagic

stroke, Ischemic heart disease, congestive cardiac failure, renal insufficiency, obstructive sleep apnoea, till cardio vascular death that continue down to at least 115/75 mmHg[1] .

Hypertension is one of the component of the metabolic syndrome and increased levels of triglycerides, cholesterol, LDL, VLDL, with decreased levels of HDL has been associated with hypertension[13]. Metabolic syndrome comprises a group of parameters that predicts the risk of occurrence of cardiovascular disease and diabetes mellitus.

Hypertension and dyslipidaemia are part and parcel of metabolic syndrome that has clearly shown to increase the risk for cardiovascular morbidity, mortality and for occurrence of diabetes mellitus.

Uric acid is one of the by-products of metabolism of purine produced in blood from endogenous purine (2/3) substances or from diet (1/3). Uric acid is considered to be one of the independent risk factor for hypertension and its levels also tend to correlate with severity of hypertension[6-12] . Uric acid is tend to have a pathogenic part in hypertension mediated by various actions such as inflammation, vascular smooth muscle cell proliferation in renal microcirculation, dysfunction of endothelium and the renin angiotensin–aldosterone system activation[4] .

Dyslipidemia has been found associated with elevation of uric acid levels and raise in any one of the lipid parameters has been found to increase the uric acid level.

Uric acid is not considered a criterion for the diagnosis of metabolic syndrome, but some studies have observed a correlation between high levels of uric acid and the metabolic syndrome in different populations[18].

Hence we here by analyse the uric acid levels in essential hypertensive individuals, lipid parameters in essential hypertensive and we seek to establish a correlation between uric acid levels and dyslipidemia in essential hypertensive individuals.

AIMS & OBJECTIVES

1. To measure the fasting serum uric acid levels in essential hypertensive individuals aged between 35 to 65 years and in healthy individuals aged between 35 to 65 years.
2. To measure the fasting serum levels of lipid parameters triglycerides, total cholesterol, LDL, VLDL and HDL in essential hypertensive individuals and healthy individuals aged between 35 to 65 years
3. To analyse the possibility of correlation existing between fasting serum uric acid levels and fasting serum lipid parameters.

REVIEW OF LITERATURE

HYPERTENSION

Hypertension is one of the leading causes of morbidity and mortality adding to the global burden of non-communicable diseases[28, 29]. It not only causes millions of deaths, but also billions of disability adjusted life years all over the world[22]. Hypertension increases the risk of cardiovascular pathology like coronary artery heart disease, heart failure, renal diseases and peripheral vascular pathology.

Its incidence is phenomenally increasing over the years, especially in developing countries rather than developed countries[1]. The awareness of this disease is quite low among people, especially among the lower socioeconomic status adding to increased mortality and morbidity. The measures to control the disease were in great vein, owing to the lack of awareness and ineffective treatment[4].

The prevalence of hypertension has been found to increase with age, owing to the vascular changes that occurs over the period of time[44]. An increase incidence of hypertension is especially seen over the age of 50 years due to the atherosclerosis of blood vessels contributing to hypertension[27].

Recent Framingham Heart Study reported that there is an increase in the hypertension in the age above 50 years and it may be due to factors such

as decreased elasticity of the arterial wall and weight gain with age[28]. Hypertension is an independent risk factor for cardiovascular morbidity and mortality.

This relation it shares with cardiovascular risk is continuous and also consistent. Studies have shown that this risk attributed to occurrence of both stroke and cardiovascular morbidity have a linear relationship from levels of blood pressure 115mm systolic and 75 mm diastolic and level of risk increases progressively from there.

This purported risk appears to be seen in all age groups starting from the age of 40 years. Systolic blood pressure when treated and decreased by 5-6 mmhg in hypertensive confers decreased relative risk of 35 to 40% for stroke and 12 to 16% for cardiovascular heart disease.

DEFINITION:

Hypertension can be defined as a level of blood pressure of 140/90 mm Hg or higher than that, and the value above which the treatment benefits seems to overcome the risks.

Prehypertension can be defined as blood pressure elevation between 120/80 and 139/89 mm Hg, so that the risk of progressing to hypertension is more when compared with the persons with blood pressure of 120/80mmhg and there is an increased risk of cardiovascular risk with that level of blood

pressure. The cardiovascular mortality rate seems to be increased, but it is unclear that the persons can benefit from treatment.

EPIDEMIOLOGY:

The prevalence of hypertension in the past in India varied differently between different populations. In rural populations it is higher with a incidence of 2 to 15 % and in relative comparison it is lesser in urban cities with a incidence of about 2 to 8%[30].

The incidence is quite going up recently in both of these areas and now it is estimated that the incidence is about 25% in urban population and 10-15% among rural population[31]. With analysis from various studies, it has been found that occurrence of coronary artery disease and stroke have increased tremendously in the population of India.

According to the study of Inter stroke and Inter heart, the occurrence of hypertension constitutes about 18% and 35% of population at risk respectively for various cardiovascular risk factors for coronary disease and stroke. There are severe regional variations noted in cardiovascular related death in India among both sexes.

The death rate has been found to be high in southern parts, north eastern areas in both sexes, while death rate found to be low in the central Indian parts of Bihar, Rajasthan and Uttar Pradesh[32,33].

The prospective phase of the on-going Million Deaths Study from 2004-2013 emphasises on regional variations and patterns of death happening in India.

All these statistics implies that there is steady rise in the number of hypertensive individuals in India, when compared with the past and it goes a steady uphill course, especially in rural areas when compared with urban population due to major unawareness.

STAGING:

Hypertension is staged according to the guidelines given by the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure - seventh report – (JNC 7)[34] .

Staging of BP	Systolic BP	Diastolic BP
Normal	<120	<80
Prehypertensives	120-139	80-89
Stage 1 hypertension	140-159	90-99
Stage 2 hypertension	≥ 160	≥ 100

TABLE 1: JNC 7 - STAGING OF BLOOD PRESSURE

In contrary to the staging given earlier by JNC VI report, a newer stage designated as Prehypertension is added . Stage 3 of hypertension which is presented in JNC VI is taken off, instead it is combined and newer staging of stage 2 with predefined value is provided.

CLINICAL DISORDERS OF HYPERTENSION:

ESSENTIAL HYPERTENSION:

Patients with hypertension without any specific underlying disorder responsible for elevation of blood pressure are categorised as ESSENTIAL HYPERTENSION. It can also be defined as Primary hypertension or Idiopathic hypertension.

SECONDARY HYPERTENSION:

Patients who have specific aetiology for the elevation of blood pressure are categorised as SECONDARY HYPERTENSION. They amount to about 5 to 20% of hypertensive population. The specific mechanism causing blood pressure elevation is more often apparent in this group of patients[36].

CAUSES OF SECONDARY HYPERTENSION:

- Renal Hypertension - Parenchymal 2-3%
- Renovascular 1 – 2%

- Endocrine Hypertension - Primary hyperaldosteronism 0.3%
- Cushing syndrome < 0.1%
- Pheochromocytoma < 0.1%
- OCP induced 2 – 3%
- Miscellaneous 1%
    - Coarctation of aorta,
    - polyarteritis,
    - neurogenic,
    - drug induced like
        - sympathomimmetics -ephedrine, phenylephrine
        - monoamine oxidase inhibitor, ergot alkaloids
        - Non-steroidal anti-inflammatory drugs
        - Glucocorticoids, oestrogen
        - caffeine
        - ethanol
        - Nicotine.

ISOLATED SYSTOLIC HYPERTENSION:

SBP ≥140 mmHg and DBP <90 mmHg.

SBP is staged appropriately as above. 0.8% in 50 years, 5% in 60 years, 12.6% in 70years, 23.6% in 80 years has isolated systolic HTN[37]. Higher in women and black subjects compared with men and white subjects.

PATHOPHYSIOLOGY:

Decrease is arterial compliance is proposed. Level of SBP is related to maximal blood flow velocity in large arteries, which in early phase of cardiac cycle, depend on heart and pulse wave velocity and in later phase depend on number of reflected waves. Pulse wave velocity is inversely related to distensibility of large artery, which is responsible for faster outflow of blood in diastole and result in decrease diastolic blood pressure.

Systolic Hypertension with Wide Pulse Pressure
1. Decreased vascular compliance (arteriosclerosis)
2. Increased cardiac output.
a. Aortic regurgitation
b. Thyrotoxicosis.
c. Hyperkinetic heart syndrome.
d. Fever.
e. Arteriovenous fistula
f. Patent ductus arteriosus

TABLE 2: SYSTOLIC HYPERTENSION WITH WIDE PULSE PRESSURE

HIGH RENIN ESSENTIAL HYPERTENSION:

Some patients with labile hypertension and mild essential hypertension have tachycardia with increased cardiac output but normal peripheral resistance. This is indicative of hyperkinetic circulation, due to beta-adrenergic activity.

Such patients have elevated plasma renin activity known as High renin Essential hypertension.

LOW RENIN ESSENTIAL HYPERTENSION:

Some patient might have low plasma rennin with high BP. But majority of them have normal plasma renin activity**.**

Secondary Causes of Systolic and Diastolic Hypertension	
Renal	Parenchymal diseases, renal cysts (including polycystic kidney disease), renal tumors (including renin-secreting tumors), obstructive uropathy
Renovascular	Arteriosclerotic, fibromuscular dysplasia
Adrenal	Primary aldosteronism, Cushing's syndrome, 17α-hydroxylase deficiency, 11β-hydroxylase deficiency, 11-hydroxysteroid dehydrogenase deficiency (licorice), pheochromocytoma
Aortic coarctation	
Obstructive sleep apnea	
Preeclampsia/eclampsia	
Neurogenic	Psychogenic, diencephalic syndrome, familial dysautonomia, polyneuritis (acute porphyria, lead poisoning), acute increased intracranial pressure, acute spinal cord section
Miscellaneous endocrine	Hypothyroidism, hyperthyroidism, hypercalcemia, acromegaly
Medications	High-dose estrogens, adrenal steroids, decongestants, appetite suppressants, cyclosporine, tricyclic antidepressants, monamine oxidase inhibitors, erythropoietin, nonsteroidal anti-inflammatory agents, cocaine

TABLE 3: SECONDARY CAUSES OF SYSTOLIC AND DIASTOLIC HYPERTENSION

WHITE COAT HYPERTENSION:

The phenomenon in which BP is elevated,in presence of health professional, while measuring BP[45]. First, described by RivaRocci more than 100 years ago. Since 24 hour ambulatory blood pressure monitoring was introduced[25], White coat hypertension was redefined as abnormal clinic BP,

but normal ABM. According to JNC- 7th, upper limit of normal ABM should be 135/85mmHg, while patient is awake and 120/75mmHg while asleep[26, 27]. WHO/ISH guidelines suggest that 24hr average of Home BP of 120/80mmHg correspond to clinic BP of 140/90mmHg.

Prevalence of WCH is 21% of all hypertensive and more likely to be females. Studies suggest WCH is associated with End Organ Damage. It should to perhaps be treated as "Pre Hypertensive State".

GENETIC CONSIDERATIONS:

Hypertension is disorder which is representative of polygenic type, in where various gene combinations along with environmental exposures to cause elevation of blood pressure. Various subsets of genes may lead to various physical characteristics linked with hypertension such as dyslipidemia and obesity[38].

On-going analysis tells that genes that represent parts of system of the renin-angiotensin-aldosterone , along with angiotensinogen and angiotensin-converting enzyme (ACE) polymorphisms, seems to be associated with causation of hypertension[39] .

Various other genes that are proposed to have association with hypertension are recently found out. Genome wide association studies

utilise scanning markers across the entire part of the genome to identify loci which are in relation with blood pressure[40].

Due to the presence of rare monogenic hypertensive diseases, the genetic variants associated with hypertension needs to be confirmed, and the various steps by which these variants affect blood pressure remain to be determined.

MECHANISMS OF HYPERTENSION:

The factors that are associated with the control of normal and increased arterial pressure have to be analysed to understand the underlying pathogenesis of hypertension. The two factors that decide the blood pressure are peripheral resistance and the cardiac output. Cardiac output is in fact contributed by the heart rate and stroke volume. The contractility of heart and vessel wall architecture and its size contributes to the stroke volume. The anatomy of small arteries and arterioles and its changes regulate the peripheral resistance.

The volume that the vessel holds decides about the pressure of the artery. The predominant ion that determines the volume of the vessel is sodium ion. when the intake of the sodium ion increased more than to be excreted by the kidney ,the volume inside the vessel increases initially and the output of the heart also increases. But if persistent amount of blood flow

has to be preserved to a particular organ, the resistance has to be increased at that site, to maintain auto regulation.

The increase in the blood pressure at first is contributed mainly by increase in the output of the heart, but as the time goes on there is an increase in peripheral resistance and the output of the heart changes to normal. The impact of sodium on the rise in blood pressure is affected by its relation it shares with chloride. The salts of sodium with no chloride content have little impact over the elevation of blood pressure[47, 48].

At first, the excretion of sodium in the urine increases due to the increase in the arterial pressure effected by the high sodium chloride intake. An increase in the rate of glomerular filtration, atrial natriuretic factor and the decline in the absorbing capacity of the renal tubules, all contribute to the pressure natriuresis effect. When the ability to excrete sodium is affected, the arterial pressure will increase and achieve natriuresis[17].

The ability of kidney to excrete sodium is affected by the intrinsic disease of the kidney, an elevated production of mineralocorticoid hormone and this contributes to sodium chloride dependent hypertension.

The absorption of sodium by the kidney is increased by the neural activity to the kidney. An increased amount of arterial pressure is required to

reach the required sodium balance. When the sodium is lost in certain conditions, the blood pressure will be low in that state[19].

AUTONOMIC NERVOUS SYSTEM:

The pressure, volume and chemoreceptor signals are the ones by which the autonomic nervous system maintains the cardiovascular stability. The regulation of blood pressure is done by the adrenergic reflexes in the recent periods, and the hormonal and other volume associated factors determine the blood pressure in long run. Norepinephrine, epinephrine, and dopamine are the three catecholamine, which are produced endogenously. The tonic and phasic cardiovascular activity is maintained by all these three endogenous catacholamines.

The G proteins are the ones which mediate the activities of the adrenergic receptors and the activity is also regulated by downstream second messengers. The agonists for adrenergic receptors subtypes with varying affinity are the epinephrine and norepinephrine. The adrenergic receptors are divided into alpha and beta depending upon their physiology and pharmacology. They are further subdivided into alpha1, alpha2,beta1 and beta2.

The number of adrenorecptors is affected by the circulating catecholamine levels. High levels of catecholamine can down regulate the

receptors in different tissues. The blood pressure is regulated constantly by several reflexes. The arterial baroreflex is regulated by stretch sensitive receptors in carotid sinus and aortic arch. These baroreceptors fire in an increasing order when arterial pressure increases and this decreases the sympathetic outflow which causes decrease in heart rate and arterial pressure. Any sudden fluctuation in arterial pressure is regulated by this mechanism. But if the patients are affected by autonomic neuropathy, these baroreceptor reflex mechanisms are blunted and they are prone to more labile blood pressure[49].

The sympathetic outflow is increased in both the normal and obese individuals with hypertension. In obstructive sleep apnea also, an increase in sympathetic outflow is observed. Sympathetic nervous system is the one which plays a vital role in the maintenance of arterial pressure.

RENIN-ANGIOTENSIN-ALDOSTERONE SYSTEM:

The regulation of arterial pressure is effected by vasoconstriction, which in turn is mediated by angiotensin II and the aldosterone which causes retention of sodium. The stimulus for renin secretion comes from three mechanisms.

1. The transport of sodium chloride when decreased into thick ascending limb of loop of henle.

2. The stretch in the renal afferent arteriole when decreased
3. The stimulation of sympathetic nervous system by adrenergic receptors. The secretion of renin is inhibited by the increased sodium chloride entry in the ascending limb of loop of henle. The secretion of renin is inhibited by angiotensin II directly and there is an increased secretion of renin when receptors of ACE is blocked[49].

Angiotensin II is a powerful pressor substance, and it stimulates the secretion of aldosterone by the adrenal zona glomerulosa. It is a powerful mitogen that growth of myocyte and vascular smooth muscle cell stimulation. Angiotension II receptors are also found in various parts of the kidney and they cause sodium excretion, dilation of vessels, formation of matrix and inhibition of cell growth. And they contribute to the maintenance of glomerular filtration rate. A block in AT I will cause an increase in AT II activity[49].

Renin mediated hypertension is observed in renovascular hypertension. The renal artery when obstructed leads on to decrease in renal perfusion pressure and thus stimulates the renin secretion. But as the time goes on, as a result of secondary renal damage, there is a less renin dependency noted in this kind of hypertension.

Even though, aldosterone secretion is increased by ACTH , it is not vital factor for chronic modulation of aldosterone

Sodium reabsorption can be affected by aldosterone by means of amiloride-sensitive epithelial sodium channels in the renal collecting duct. Sodium is exchanged for potassium and hydrogen ions and hence electric neutrality is regulated by aldosterone. So hypokalemia and alkalosis can occur by increase in secretion of aldosterone.

Non epithelial cell are also affected by aldosterone. It causes changes in structure and function in vital organs including kidney, heart, blood vessels resulting in varied consequences such as fibrosis of myocardium, nephrosclerosis, inflammation of vessel wall and remodelling due to oxidative stress

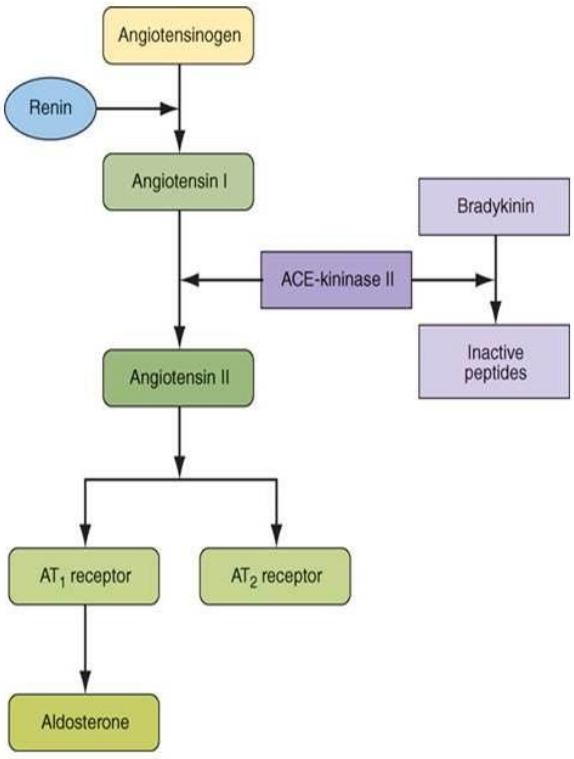


FIGURE 1: Renin angiotensin aldosterone axis

The elevated action of the renin-angiotensin-aldosterone axis has been associated with hypertension invariably. Whenever there is a decreased sodium chloride diet is taken, or when a volume contraction occurs, there is an increased action of renin angiotensin aldosterone axis and there by maintaining the arterial pressure. A secondary elevation of aldosterone also occurs in edematous states such as congestive cardiac failure and liver disease[103].

VASCULAR MECHANISMS:

The radius of vessel and the compliance of arteries play a vital role in the determination of arterial pressure. The blood flow is inversely proportional to the size of the lumen and hence the small changes in the size of the vessel will influence the resistance. The changes in functional, structural and mechanical levels in hypertensive patients will cause the lumen diameter to be reduced and hence causing the elevation of blood pressure. When alterations in vessel wall happen without variation in vessel volume, it will result in remodelling.

There is an increase in peripheral resistance noted due to hypertrophic or eutrophic remodelling. Low-grade inflammation, vascular fibrosis and apoptosis will also influence remodelling. The elasticity of the vessel will also influence the lumen diameter.

The arterial stiffening and arteriosclerosis in the hypertension causes high systolic blood pressure and decreased vascular compliance due to structural changes can cause a wide pulse pressure. The stiffness of arteries can independently predict the risk of cardiovascular events.

The transport of ions in vascular smooth muscle cells influence the vascular tone and growth, and hence causing the elevation in blood pressure. These vascular tone and vascular growth is modulated by in trace.

The vascular tone is modulated by endothelial function and nitric oxide modulates the vascular tone by causing vasodilation. There is an impairment of endothelium dependent vasodilation that occurs in hypertensive. A vasoconstrictor called Endothelin is synthesised by the endothelium, and the antagonists of endothelin may decrease the blood pressure in individuals with resistant hypertension.

MEASUREMENT:

Sphygmomanometer is the instrument used to measure BP. Both mercury and aneroid types are used. But sometimes reading were found inaccurate, unreliable due to extreme bouncing, illegibility of gauge, blockage of the filter, lack of mercury in reservoir, bladder damage, rubber aging and leaks[50]. So these things have to be corrected before recording BP.

The movement of the arms can cause notable artefacts in measurement of blood pressure, systolic pressure becomes higher. Guidelines given by the world health organisation recommended that cubital fossa should be kept at the level of 4^{th} ICS[51].

The American Heart Association states the heart level as "Arbitrarily taken to the junction of 4^{th} ICS and lower left sternal border. Practical clinical guide defines it as "When the patient is seated placing the arm on a nearby table top, a little above waist level is the satisfactory position[52].

Home measurements by patients itself is similar to ambulatory BP monitoring. ABM is acceptable to patients. But self-measurement is not possible[50]. Several studies show that measurement of blood pressure in home and by giving numerous recordings of blood pressure under relatively stable condition is beneficial and there by evading White Coat hypertension, and so considered superior to hospital measurement, in terms of association with organ damage, rehabitility and assessing the predictive value of cardiovascular pathology .American Heart Association found that not one of 114 participating cardiologist followed all techniques of office BP recording.

DETERMINANTS OF HYPERTENSION:

1. WEIGHT GAIN

It is major controllable risk factor for new onset of HTN. Abdominal obesity as evidenced by waist circumference of ≥ 85 cm in women &≥98cm in men. 1mmHg of SBP rise for every 2 Lb weight gain.

2. SALT INTAKE

Salt sensitivity is in raise with BP. BP increase with salt intake and BP decreases with salt restriction[47]. It is common in black. Salt that is consumed in the diet regulates the production of transforming growth factor beta in the kidneys that is linked to hypertension related cardio-renal complication. TGF –ß was observed to be increased in black individuals with incidence of hypertension.

3. ALCOHOL INTAKE

Consumption of low to moderate amount of alcohol also associated with a high risk of hypertension in blacks. Alcohols accounts for 5-30% of all HTN.

4. PHYSICAL ACTIVITY

Sedentary individuals have 20 – 50% increase risk of developing hypertension. Regular exercise lowers BP.

5. SMOKING

Smoking reported to cause acute rise of BP. However relationship between smoking and level of BP is not reported.

6. SOCIOECONOMIC STATUS

Hypertension has more prevalent in upper socio economic group and developed countries.

Improving lifestyles is key in treatment, not just pharmacologic therapy, National recommendation and legislation of Finland, include labelling salt content of commercial prepared food and use potassium, magnesium enriched minerals salt instead of common salt in home and food industry.

7. EFFECT OF EXERCISE

There is an inverse relationship between physical activity and BP. The effect of exercise is more pronounced in hypertensive than in normotensives.

However exercise is less effective than diet in lowering BP. The vascular resistance of systemic circulation is decreased due to exercise.

Because of the vasodilatation in working muscles, there is an increase in the output of the heart and a marginal rise in diastolic and notable rise in systolic blood pressure is noticed. Once when exercise is over, the output of

the heart decreases fastly and this will lead on to decrease in the blood pressure than prior to exercise.

Along with these vasodilatory mechanisms, a decrease in the activity of the sympathetic nervous system is also observed.

So in order to prevent and effectively treat hypertension, modification of life style and behavioural changes are needed in the form of aerobic exercises done regularly and consistently, a decreased dietary sodium intake weight loss and moderate intake of alcohol.

SYMPTOMS AND SIGNS:

HISTORY:

The hypertensive patient must be evaluated with a good history and thorough examination to validate the diagnosis of hypertension initially and then a systematic and methodical examination is done to find the secondary causes that contribute to hypertension, assessing the risk factor for cardiovascular disease, to find the complications and the end organ damages caused by the hypertension.

History pertaining to any particular life style, that poses a threat to the causation of hypertension, so that a life style modification and behavioural therapy can be given.

Most of the individuals in which the hypertension was diagnosed show no particular symptoms pertaining to their increase in the blood pressure. When the blood pressure elevation is severe in the patients, they usually complaint of headache. The headache occurs especially early in the morning and it occurs in the back of the head at the occipital region.

Many other symptoms can occur in hypertension and they are considered nonspecific. Easy fatigability, palpitations, dizziness, impotence can be present in individuals with elevated blood pressure and they are considered nonspecific.

When the patients have specific symptoms, it usually denotes there is a underlying cause for the elevation of blood pressure and so it can be observed that patient can have secondary hypertension[49].

Patient's Relevant History
Duration of hypertension
Previous therapies: responses and side effects
Family history of hypertension and cardiovascular disease
Dietary and psychosocial history
Other risk factors: weight change, dyslipidemia, smoking, diabetes, physical inactivity
Evidence of secondary hypertension: history of renal disease; change in appearance; muscle weakness; spells of sweating, palpitations, tremor; erratic sleep, snoring, daytime somnolence; symptoms of hypo- or hyperthyroidism; use of agents that may increase blood pressure
Evidence of target organ damage: history of TIA, stroke, transient blindness; angina, myocardial infarction, congestive heart failure; sexual function Other comorbidities

TABLE 4: Relevant history in hypertension

PHYSICAL EXAMINATION:

In a hypertensive individual, height of the patient measured, weight of the patient weighed and then body mass index calculated to observe any obesity. The blood pressure is measured in both the upper limbs and it is also taken with patient in supine, lying and standing position, to observe for the occurrence of postural hypertension.

The blood pressure should also be taken in the lower limb once, if the individual is young and his age is below 30 years. The heart rate should also be counted in the patient.

The pulse should be palpated for any irregularity, since in hypertensive patients, an increased incidence of atrial fibrillation is found out. The patient neck is examined and observed for any enlargement of the thyroid gland and patient looked for any signs pertaining to hypothyroidism and hyperthyroidism.

Patient should be examined for any bruits present for carotid and femoral arteries, his fundus should be examined with fundoscope and femoral, dorsalis pedis pulse should be palpated. When doing a fundsocopic examination any increase in the arteriolar light reflex, arteriovenous crossing anomalies, retinal hemorrhages, cotton wool spots and hard exudates has to

be seen, since they can imply about the severity of hypertension. Papilloedema can be observed in patient with malignant hypertension.

In the cardiovascular examination, one can observe a loud second heart sound, S4 gallop due to the noncompliance of the left ventricle. The apical impulse when palpated will be displaced down and out, and it will be well sustained in nature.

When you can auscultate an abdominal bruit, a possibility of renovascular hypertension can be considered. When kidneys are palpable in examination of abdomen, then possibility of polycystic kidney should be considered.

Any other signs of heart failure should be found out and thorough neurological examination should also be carried out to exclude neurological causes.

INVESTIGATIONS:

24 hrs urinary sodium excretion and sodium/potassium ratio are strongly associated with BP. Serum ionized calcium concentration was decreasing significantly in elderly subjects and it worsened their prognosis. High LDL concentration in seen in elderly hypertensive. Negative correlation between ionized calcium and triglyceride were found in young and elderly hypertensive. In young, non-dippers (BP doesn’t fall nocturnally)

suggest poor cardiovascular prognosis.

Basic Laboratory Tests for Initial Evaluation	
System	**Test**
Renal	Microscopic urinalysis, albumin excretion, serum BUN and/or creatinine
Endocrine	Serum sodium, potassium, calcium, ?TSH
Metabolic	Fasting blood glucose, total cholesterol, HDL and LDL (often computed) cholesterol, triglycerides
Other	Hematocrit, electrocardiogram

TABLE 5: Laboratory investigations in hypertension

AGING AND HYPERTENSION:

Structure and function in the microcirculation get altered and they are vital factors contributing to pathology in vascular disease such as hypertension. Capillary pressure is rises in primary hypertension, and this is due to decrease in number of capillaries or pathology in vascular responses at a precapillary or postcapillary level.

Both capillary rarefaction and altered responses in microvasculature have been seen before the onset of clinical hypertension, implicating their part in etiology.

Aging has been associated with dysfunction of endothelium, because of a decrease in NO and prostanoid pathways.

In aging, however hypertension is largely contributed due to altered large artery stiffness.

MONOGENIC HYPERTENSION:

Various forms of monogenic hypertension have been found out. They are found by their characteristic phenotypes, and the diagnosis may be confirmed by genetic analysis. Different inherited disorders in adrenal steroid biosynthesis lead to mineralocorticoid-induced hypertension and hypokalemia. In 17-hydroxylase deficiency, sex hormones and cortisol is not synthesised adequately. Their sexual maturation is at stake. Males could present as pseudo hermaphrodite and females could present as primary amenorrhea and absent secondary sexual characteristics.

Increased synthesis of mineralocorticoids will lead on to hypertension, especially when enzymatic block occurs proximally, leading on to accumulation of desoxycorticosterone. An 11-hydroxylase deficiency leads to increased synthesis of mineralocorticoids and diversion of steroid synthesis into the androgen pathway. An 11-hydroxysteroid dehydrogenase deficiency has an impaired ability to metabolize cortisol to its inactive metabolite and this leads on to hypertension.

This defect could be acquired, and in some cases inherited and may be due to licorice-containing glycyrrhizin acid. The same substance is present in the chewing tobacco paste of several brands.

The Liddle's syndrome occurs due to constitutive activation of amiloride-sensitive epithelial sodium channels present on the distal renal tubule, resulting in excess sodium reabsorption; in pregnancy exacerbation of hypertension occurs because of activation of the mineralocorticoid receptor by progesterone.

COMPLICATIONS OF HYPERTENSION:

Hypertension if found out has to be treated promptly, otherwise lack of treatment can result in dire consequences. Hypertension can result in mortality due to coronary artery heart disease, heart failure, stroke and renal failure if not treated properly.

When the elevation of blood pressure is rapid, and if it is in an accelerated fashion then patient can due to renal failure frequently.

OPHTHALMIC CHANGES IN HYPERTENSION:

The only tissue in the body in which arteries, arterioles, veins that can be visualised directly is the retina of the eye.

Changes in the arteries and veins can show the severity of hypertension and thereby we can grade the retinopathic changes according to the severity.

Fundoscopic examination is thus helpful in treating the potential retinopathic changes as well as the severe hypertension when present can be brought to the notice by this examination.

The retinal changes in hypertension is graded by various systems and one among them is the The Keith Wagener Barker classification and it grades the severity of hypertension according to the fundoscopic changes seen.

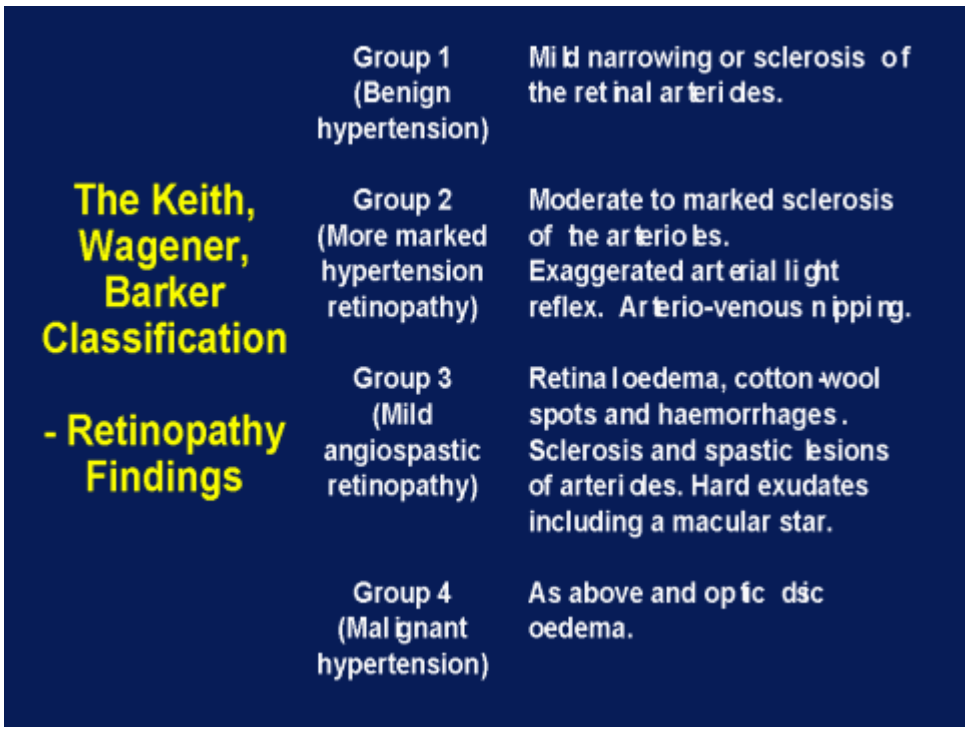


TABLE 6: The Keith Wagener Barker Classification of Hypertensive Retinopathy

HYPERTENSION AND HEART:

The stiffness and hypertrophy occurs in the heart because of the undue tension on the myocardium of the left ventricle and this increases the development of atherosclerosis in the vessel walls of the heart. Left

ventricular systolic function is compromised in long run and initially patient has diastolic function of the heart compromised with lower E/A ratio and increased isovolumetric relaxation time.

These changes can be visualised and observed in the echocardiogram.

LEFT VENTRICULAR HYPERTROPHY:

Hypertrophy of the left ventricle of the heart occurs due to the elevated afterload with which heart has to contract against. This is in due course can result in left ventricular systolic dysfunction.

An abnormal diastolic filling pattern of the left ventricle and left ventricular wall mechanics appears to be compromised when seen in echocardiogram. The vasodilatory capacity of the coronary arteries gets reduced often.

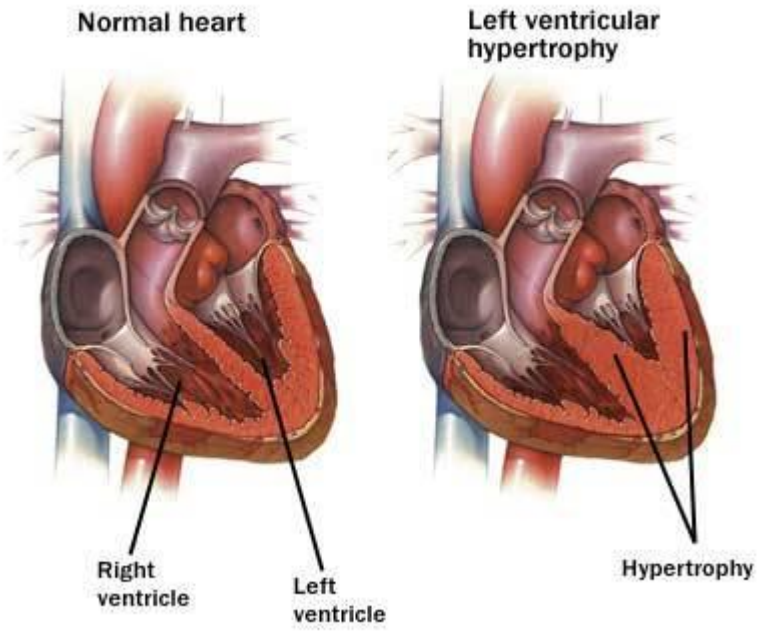


FIGURE 2: Left ventricular hypertrophy

HEART FAILURE:

The left ventricular systolic dysfunction and the diastolic dysfunction will affect the capacity of heart to pump the adequate blood out and this can result in heart failure. An increment in the systolic blood pressure increased the risk of patient developing heart failure according to the Framingham heart study[96].

When the left ventricular systolic dysfunction is severe, the ejection fraction starts falling and due to the decreased compliance of the left ventricle patient ultimately goes to the pulmonary edema if the hypertension not treated promptly.

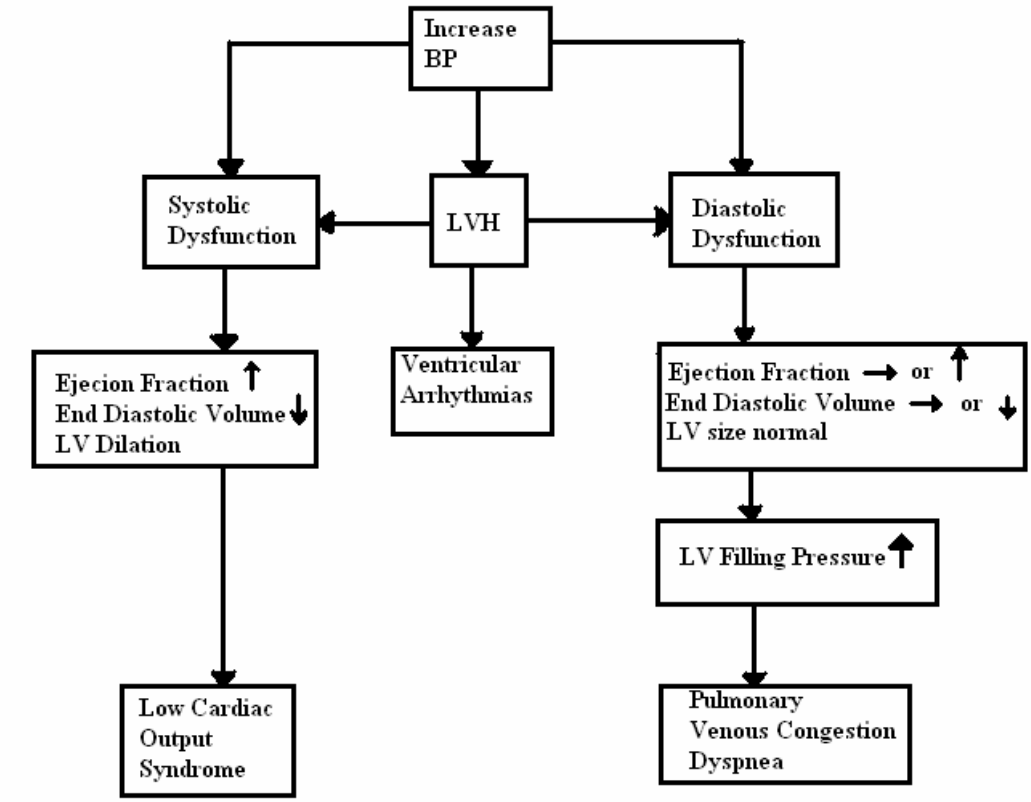


FIGURE3: Complications of hypertension

FIGURE4: Concentric hypertrophy of the heart seen in hypertensive patient

CORONARY HEART DISEASE:

Hypertension is one of the important factors posing a risk for the patient to develop coronary artery heart disease and myocardial infarction. Uncontrolled hypertension will result in the coronary angina pain and will result in cardiovascular morbidity and mortality.

The prognosis of the coronary heart disease and myocardial infarction also depends upon the blood pressure which is present before and it is also influenced by the control in the near future. The myocardial infarction can occur silently and this proportion seems to be increased in the hypertensive population rather than in normal population.

The silent myocardial infarction can result in sudden cardiac death and they are at increased risk for the cardiovascular morbidity and mortality.

HYPERTENSION AND KIDNEYS:

An unnoticed small dysfunction of kidneys will result in the development of primary hypertension. Recently kidneys are the targets of research in searching for the etiology of primary hypertension especially the pressure natriuresis effect in the kidneys. Any renal mishandling of salt and water will result in the retention of salt and consequently solvent retention resulting in the development of hypertension.

The hypertensive individuals show microalbuminuria which indicates the underlying structural and functional dysfunction causing the intraglomerular hypertension.

Whenever microalbuminuria is seen in hypertensive individuals, they should be evaluated for left ventricular hypertrophy and carotid artery thickness, since they show a strong correlation with each other.

When nephroscleosis happens as a result of ongoing hypertension, the plasma creatinine level will be elevated indicating the renal failure and patient goes in for complete renal insufficiency.

HYPERTENSION AND CENTRAL NERVOUS SYSTEM:

Cerebrovascular accidents are found with an increasing incidence in patients with hypertension. Ischemic stroke as well as hemorrhagic stroke tends to be increased in hypertensive individuals and hypertension is one of the independent risk factor for the occurrence of stroke.

Lacunar infarcts are more common in patients with hypertension. White matter lesions in cerebral cortex have been picked up in MRI BRAIN about 45%.

Most of the strokes due to hypertension are due to infarction and others are because of intracerberal haemorrhage or subarachnoid haemorrhage. When the hypertensive individual is above 65 years, the risk of the patient developing stroke is very high due to the proportional increase in blood pressure with age.

Impairment of cognition has been found in the hypertensive patients and this is attributed to multiple lacunar infarcts due to small vessel disease culminating in white matter dementia.

In patients with hypertension, when blood pressure elevated beyond a certain level, auto regulation of cerebral blood flow is lost and patient lapses into encephalopathy.

When hypertension not promptly treated, patient will progress in to stupor, coma and even death within hours. Care must be taken to differentiate hypertensive encephalopathy from other neurological disorders,

so that appropriate treatment will save the life of the patient.

HYPERTENSION AND PREGNANCY:

Hypertension in pregnancy usually appears after 20 weeks of gestation and about 15% of these conditions develop in previously normotensive women. Nearly 50% of these women will go on for preeclampsia which is complicated with pedal edema, proteinuria with risk of going into eclampsia which is complicated by seizures.

In individuals with history of hypertension before pregnancy, they are at more risk for developing preeclampsia and eclampsia when compared with normotensive women developing hypertension.

Women who are progressing for preeclampsia are at higher risk of delivery small for gestatiaonal babies due to a placental compromise.

DYSLIPEDEMIA

LIPIDS:

Definition: Lipids are compounds relatively insoluble in water, but freely soluble in non-polar organic solvents like Benzene, Ether etc.,

CLASSIFICATION:

1. SIMPLE LIPIDS: They are esters of fatty acid with glycerol or higher alcohol[66].

A. Triacylglycerol

B. Wax

2. COMPOUND LIPIDS: They are fatty acid esterified with alcohol, but in addition contain other groups

a) . Phospholipids like

- ❖ Lecithin
- ❖ Cephalin
- ❖ Phosphatidyl Serine
- ❖ Phosphatidyl Inositol
- ❖ Phosphatidyl Glycerol
- ❖ Plasmalogens
- ❖ Sphingomyleins

b). Non Phosphorylated Lipids

- ❖ Glycolilpids - Cerebrosides
- ❖ Globosides

- ❖ Gangliosides
- ❖ Sulpho Lipides

3. DERIVED LIPIDS: Compounds derived from lipids or precursors of lipids

Eg. Fatty Acid, Steroids, Prostaglandins, Leukotrienes, Terpenes, Dolichols etc.,

4. LIPID COMPLEX : Proteolipids and Lipoproteins[101].

FUNCTION OF LIPIDS:

1. Storage from of energy – Triacyl glycerides
2. Structural components of Bio membranes – Phospholipids Cholesterol
3. Providing Insulation against changes in external temperature – Subcutaneous fat.
4. Giving shape & contour to the body
5. Protecting internal organs by providing a cushioning (Pads of fat)
6. Metabolic regulators (steroid, Hormones, Prostaglandin)
7. Acting as surfactants, detergents, emulsifying agents
8. Acting as Electric insulators in neurons.
9. Help in absorption of Fat soluble vitamins (A, D, E, and K)
10. Add taste & palatability to food.

LIPID METABOLISM:

Triacylglycerides or Triglycerides are esters of glycerol, containing 3 fatty acids attached to 3 Carbon alcohol of glycerol. Both animals & plants are the source of triglycerides. Triglycerides from plants have long chained unsaturatedfatty acids. So it is liquid at room temperature. But animal triglycerides have medium chain saturated fatty acids. So, solids at room temperature[112].

METABOLISM OF TRIGLYCERIDES:

Triglycerides are digested in duodenum and proximal ileum. Pancreatic and intestinal lipase hydrolyse to glycerol, monoacyl glycerol and fatty acids. After absorption, Triglycerides are resynthesied in intestinal epithelial cells and combine with cholesterol and Apo B-48 to form Chylomicrons. Chylomicrons are secreted to lymphatic system travel through thoracic duct and reach blood stream through Jugular vein.

LIPOPROTEIN

DEFINITION:

Lipids synthesis in liver & intestine are insoluble. So they are transported to various tissues for metabolic functions through formation of macromolecular complex called Lipoproteins. They are spherical particles with nonpolar lipid core containing Triglycerides and cholesterol esters. Peripheral polar lipid contains phospholipids and free cholesterol near surface[101].

They also contain specific proteins called Apolipoproteins located on surface. They are non-covalently attached through hydrogen bond and vander waals force.

Binding of lipids to protein is loose enough to allow ready exchange of lipids among the plasma lipoprotein and between cell membranes and lipoprotein[64].

TYPE OF LIPOPROTEINS:

Based on hydrated densities, separated by ultra-centrifugation:

- Chylomicrons
- Very low Density Lipoprotein
- Intermediate Density Lipoprotein
- High Density Liproprotein
- Lipoprotein a.

APOLIPOPROTEINS:

It is protein component of lipoproteins. They are present in various proportions in all lipoprotein.

- Apo A-I, Apo A-II, Apo A IV
- Apo B-100, Apo B-48
- ApoC-1,ApoC-II,ApoC-III
- Apo-E,
- Apo (a)

FUNCTION OF APOLIPOPORTEIN:

1. Activating important enzymes in lipoprotein metabolic pathway.

2. Maintain structural integrity of lipoprotein complex

3. Facilitating uptake of lipoprotein into cells through their recognition by specific cell surface receptors[62].

COMPOSITION OF LIPOPROTEIN

Lipoprotein	Source	Diameter (nm)	Density(g/dl)	Protein %	Lipid %	Components
Chylomicrons	Intestine	90-100	<0.95	1-2	98-99	Triacylglycerol
Chylomicron remnants	Chylomicrons	45-150	<1.006	6-8	92-94	Triacylglycerol,phospholipids, Cholesterol
VLDL	Liver(intestine)	30-90	0.95-1.006	7-10	90-93	Triacylglycerol
IDL	VLDL	25-35	1.006-1.019	11	89	Triacylglycerol,Cholesterol
LDL	VLDL	20-25	1.019-1.063	21	79	Cholesterol
HDL 1	Liver,intestine, VLDL, Chylomicrons	20-25	1.019-1.063	32	68	Phospholipids, cholesterol
HDL 2		10-20	1.063-1.210	33	67	
HDL 3		5-10	1.125-1.210	57	43	
Albumin/FFA	Adipose tissue		>1.281	99	1	Free fatty acid

TABLE 7: Composition of lipoprotein

LIPOPROTEIN METABOLISM

PATHWAYS OF LIPOPROTEIN METABOLISM

1) Endogenous pathway

2) Exogenous pathway

3) Intracellular LDL receptor

4) HDL Reverse – Cholesterol pathway

1. EXOGENOUS PATHWAY (CHYLOMICRON):

Lipoprotein is of dietary origin. Dietary triglycerides & Cholesterol esters are assembled in secretary vesicles in Golgi apparatus to form Nascent-chylomicrons. It is introduced into circulation through intestinal villi. It's lipid content is 90% of Triglyceride and 2% of Apo B-48 and Apo A. This Nascent-chylomicron acquires Apo C and Apo E from HDL to form Chylomicron.

Apo C-II present on surface of chylomicron activates lipoprotein lipase, attached to luminal surface of endothelial cells. Lipoprotein lipase hydrolysis triglycerides to free fatty acids, which can be taken up by muscle for energy or adipose tissue for storage.

ApoA and some phospholipids & free cholesterol are transferred from chylomicron to HDL. This newly formed chylomicron is called chylomicron-Remnant containing 80% TGL, % Apo B-8 & Apo E.

Presence of Apo B-48 & Apo E is recognized by specific hepatic remnant receptor and internalized by endocytosis. Lysosyme hydrolyse chylomicron remnants & from bile acids. This is incorporated into newly formed lipoprotein or stored as cholesteryl ester.

2. ENDOGENOUS PATHWAY:

Lipoprotein is of hepatic origin. Triglycerides, Cholesterol can be synthesised in liver. This endogenous Triglyceride and cholesterol are packaged in secretary vesicles in Golgi apparatus, transported by exocytosis

into ECF & then into circulation, in the form of Nascent VLDL, containing 55% TGL & Apo B-100, Apo E, small amount Apo C on its surface. Additional Apo E and Apo C are transferred from circulating HDL to nascent VLDL forming VLDL. Apo CII present on surface of VLDL activates LPL on endothelial cells and hydrolysis VLDL-TGL releasing free fatty acids and glycerol.

During hydrolysis Apo C is transferred back to HDL. VLDL is converted to VLDL remnants some are taken up by liver and rest converted to IDL. IDL has Apo E on surface, so bind to hepatic remnant receptor removing 50% of IDL. Some materials from IDL, that is phospholipids, free cholesterol, and apolipoprotein are transferred to HDL to form HDL-Denova. Cholesteryl esters are transferred from HDL to LDL.

Net result of lipolysis and cholesteryl esters exchange is replacement of triglyceride core of VLDL with cholesteryl esters. Further IDL undergoes lipolysis removing of remaining triglycerides and all apolipoproteins except B-100 to form LDL.

3. LDL RECEPTOR PATHWAY:

Specific receptors present in coated pits of plasma membrane recognize and bind to apo B-100 of LDL. The particles are internalized in coated vesicle to form endosome. Receptor dissociates from LDL and return to cell surface. LDL migrate to lysosome, Apo- B 100 is degraded to small peptides and amino acids.

Cholesterol esters are hydrolysed and free cholesterol is available for synthesis of cell membranes, steroid hormones and bile acids.

Over supply of free cholesterol leads to:

1. Decreased rate of endogenous synthesis of cholesterol by inhibiting rate limiting enzyme HMG-COA reductase.
2. Increased formation of cholestryl esters catalysed by ACAT.
3. Inhibition of Synthesis of new LDL receptors by suppression of transcriptionof receptor gene.

LDL is also taken up by extra hepatic tissues through scavenger receptors or nonreceptor mediated pinocytosis. The nonreceptor mediated uptake become significant as plasma concentration increase as in case of familial hypercholesterolemia.

Nonreceptor mediated uptake is not saturated or regulated. Scavenger receptor is also unregulated, found in macrophages and other cells. Macrophages engorge cholesteryl esters and form foam cells, considered the earliest component of atherosclerotic lesion. 2/3rd of LDL is removed by LDL receptors and remaining by scavenger cell system.

4. HDL – REVERSE CHOLESTEROL TRANSFER PATHWAY:

HDL secreted from liver or intestine as disc-shaped nascent particle consist of phospholipids and ApoA-1. Triglyceride rich particles such as phospholipids, cholesterol and certain apolipoprotein get added to nascent HDL, to form spherical particles called HDL3. Cholesterol is esterified by

action of lecithin cholesterol acyl transfers (LCAT) in presence of cofactor apoA-1. So size of HDL depend on amount of accumulated

cholesterol esters and activity of LCAT This form HDL2.

HDL cholesteryl esters are delivered to liver by following mechanisms:

1. Cholesteryl esters from HDL are selectivity taken by hepatic HDL receptors. HDL particles are returned back to circulation.
2. Cholesteryl esters are transferred from HDL to Apo B-100 lipoprotein and further taken up by liver through receptors of lipoprotein. This is mediated by CETP (Cholesterol Ester Transfer Protein)
3. HDL Apo E is also recognized by hepatic receptors. This process delivers cellular and lipoprotein cholesterol back to liver for use or disposal. So, called Revenue cholesterol transport system.

FIGURE 5: EXOGENOUS PATHWAY

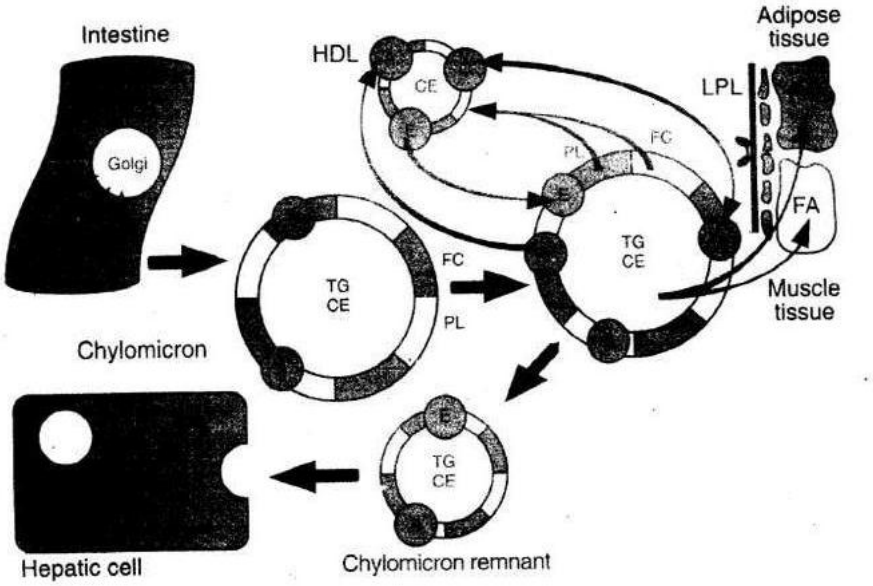


FIGURE6: ENDOGENOUS PATHWAY

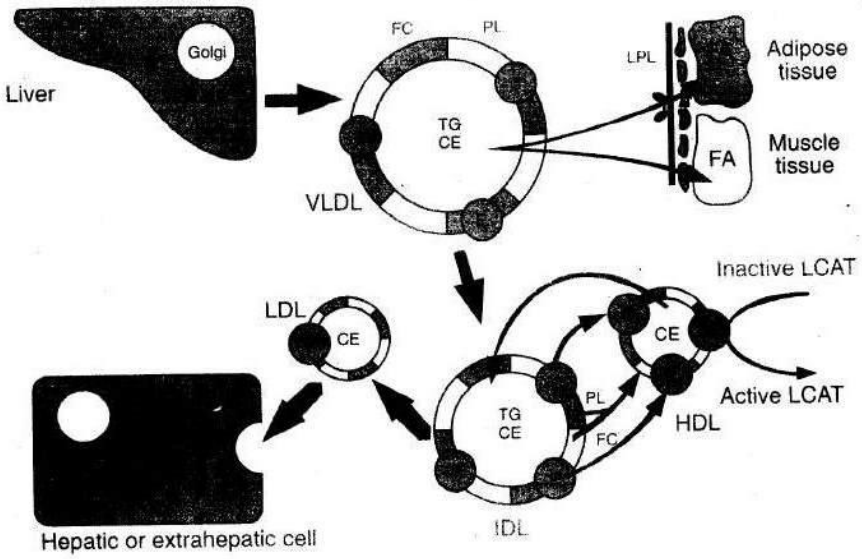
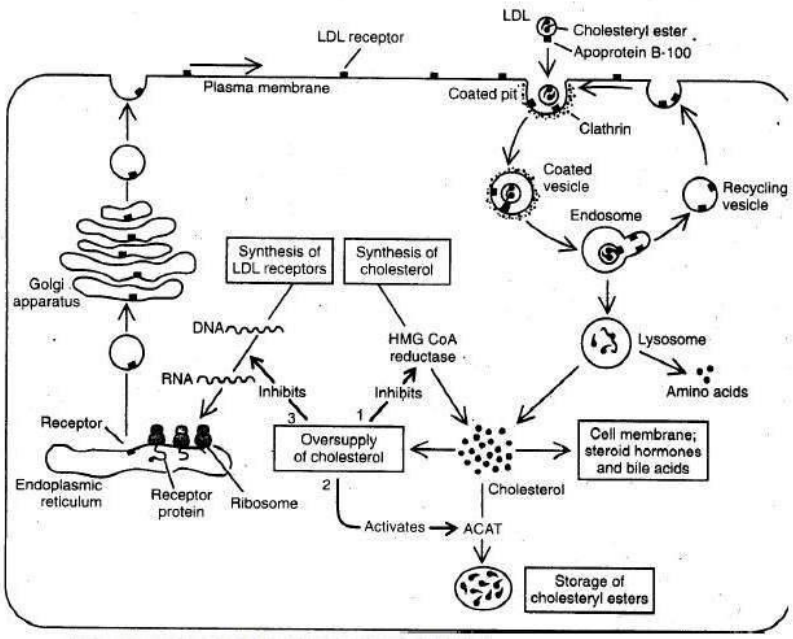


FIGURE 7: LDL RECEPTOR PATH WAY



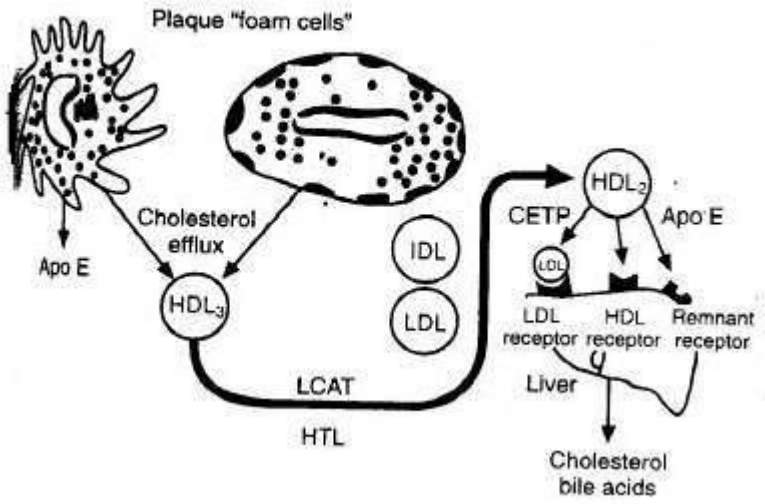


FIGURE 8: REVERSE CHOLESTEROL TRANSPORT

CLINICAL SIGNIFICANCE OF LIPIDS:

High levels of lipids easily lead to atherosclerosis, a cause of CHD. The association between serum cholesterol and atherosclerosis in human was suggested in1983. Familial aggregation of hyper cholesterolemia and CHD was also demonstrated.

Risk ratio between atherosclerotic coronary disease and cholesterol is 1 at 200 mg/dl of cholesterol value. Ratio increase to 2 at 250 mg/dl and 4 at 300 mg/dl 53. Increased fasting hypertriglyceridemia, hypercholesterolemia, increased LDL and decreased HDL is associated with increased risk with CHD[61]. A reduction of LDL cholesterol is correlated with regression in atherosclerotic lesion in individual with CHD. Increased ApoB-100 and decreased Apo A-I is seen with CHD[62].

CHD is increased by saturated fatty acid and by mono and poly unsaturated fatty acid. BP is associated with dietary intake of saturated facts and inversely with dietary intake of linolenic acid. Level of palimitoleic acid in serum cholesterol esters, which is supposed to reflect dietary saturated facts, was associated with hypertension[54].

Lower level of plasma linoleic acid high plasma level of palmitic and arachidonic acid are associated with higher risk of hypertension. Arachidonic acid may act through changes in eicosanoid and prostaglandin metabolism. They also balance between thromoboxan A2 (vasoconstrictor) and prostacyclin (vasodilator) .

Higher plasma concentration of lipoprotein (a), albeit within normal range could be independent risk factor for atherosclerosis and could contribute towards, increasing incidence of cardio vascular disease in people with essential hypertension[60]. However routine measurement of Lp(a) in hypertension should perhaps be simply regarded as research exercise, because there is limited data on prognostic and predictive value in hypertensive[59].

Very few therapeutic manoeuvres can reliably used to lower Lp (a) which no clear evidence of benefit perhaps routine lipid profile is more appropriate.

Hyper triglyceridemia in mild hypertension is indicative of insulin resistance accompanied by a modified vascular reactivity as well as elevated catecholamine and adreno cortico trophic hormone.

Hypertriglycerduria in HUCIIITg mice appear to result primarily from decreased tissue uptake of triglyceride rich particle from the circulation, which is most likely due to increased Apo CIII and decreased Apo E on VLDL particles.

Oxidised LDL cholesterol is vasoconstrictor, mitogenic, pro-inflammatory and thrombogenic[63]. LDL cholesterol potentiates noradrenalin vasoconstriction in the peripheral vasculature and in the coronary, cerebral and renal vascular beds[53]. There is also blunting of endothelium dependent vasodilator responses to acetylcholine[63].

High Cholesterol has shown in impair endothelium dependent dilation. Cholesterol levels influence BP response to adrenergic stimulation as well as outcome of target organ disease. Lipoprotein strongly contribute to atherogenesis might play a relevant role in pathophysiology of hypertension. Total cholesterol is important single blood lipid risk factor for ischemic heart disease is men. HDL-cholesterol is less important and triglyceride concentration does not have predictive importance once other risk factors have been taken its account.

Similar study showed total cholesterol and triglyceride were positively correlated. HDL-cholesterol was inversely correlated with triglyceride. HDL cholesterol and total cholesterol were not correlated. There is a strong association between apolipoprotein E locus, hypertension and lipid profile. Thyroid hormones were reported to be capable of inhibiting atherosclerosis in animals and lowering blood cholesterol[56]. Lipid lowering drug with antihypertensive will reduce BP and cardiovascular risk event. Other study showed no substantial associated between antihypertensive therapy and plasma lipid levels [64].

NORMAL VALUES OF LIPID PROFILE:

Triglyceride - 30 -200 mg/dl

Total cholesterol- 150-200 mg/dl

LDL- 70-130 mg/dl

HDL 40-60 mg/dl

VLDL 20-40 mg/dl

URID ACID

Metabolism:Uric acid is derived from catabolism of

ingested nucleoproteins

-endogenous nucleoproteins

endogenous purine nucleotides.

Uric acid is a breakdown product of purine metabolism. It is produced in liver and excreted through kidney. Uric acid is completely filtered through glomerulus almost fully reabsorbed at proximal convoluted tubule and actively secreted along the tubule. Also, catabolised to urea, ammonia and finally carbon di oxide.

Total body content in average adult is 1.2 g

Plasma uric acid is 3.5 – 7mg/dl in males

2.7 – 6.5 mg/dl in females[96].

Average Adult excretes 400 – 600 mg in 24 hrs urine.

On low purine diet 275 – 600 mg is excreted

In Gout increase to 18000 – 30000 mg (total content)

GOUT:

Clinical condition, in which uric acid is increased.

• Primary Gout - Ribose Phosphate phosphorylase is deficient.

• Secondary Gout - Due to increased purine catabolism seen in leukemia, prolong fasting, polycythemia.

• Renal Gout - Uric Acid transport System is affected, resulting in failure of excretion.

• Secondary Renal Gout seen in generalized renal failure[106].

CLINICAL SIGNIFICANCE OF URIC ACID:

Hyperuricemia is seen in

- ❖ Renal failure
- ❖ Ketoacidosis
- ❖ Lactate Excess
- ❖ Pre eclampsic toxemia with increased lactic acid
- ❖ Diuretics

Positive relationship of Hyperuricemia to hyperlipidemia is seen in following conditions:

- ❖ Obeisty
- ❖ Atherosclerosis
- ❖ Diabetes mellitus
- ❖ hypertension
- ❖ Exercise

- ❖ Achievement oriented behaviours
- ❖ Diet with high purine like meat, viscera, leguminous vegetable and yeast.

In mammals, uric acid is degraded to allantion by uricase resulting in uric acid levels to 0.5 – 1.5 ml/dl, whereas in Hominoids (apes, Humans) uric acid level is high due to distinct mutation in uricase gene, that made it non-functional. Three mutations are nonsense mutation occurring at codon 33, a non sense codon 187 and slice mutation inexon 3 .

Hypeuricemia occur as a result of either overproduction or under excretion of uric acid or both[67]. Over production occur with rare genetic disorders. Alcohol consumption, high purine intake, haematological malignancies release high purine. Under excretion is clinically significant seen in diuretic treated hypertensive.

Impairment of renal function may cause hyperuricemia through reduction in both filtration and secretion of uric acid. Raised S. uric acid can be the consequence of an increased urate production, a decreased renal excretion or both[69].

But studies showed that UA is positively correlated with S.creatinine but not in patients with under excretory hyperuricemia.20-40% of patients with essential hypertension are hyperuricemic.

Uric acid is implicated in pathogenesis of hypertension[74]. There is positive relationship of UA to hypertension[72].

Raise in SBP by 30-40 mmHg will increase UA by 1 mg/dl. 9yrs follow up study showed positively associated with incident hypertension and UA. This relationship was stronger in Blacks than in whites. 10 yr incidence of HTN in a population based cohort study showed positive association between UA & hypertension

A Normative aging study also showed positive relation after adjusting for age BMI, abdominal circumference, smoking alcohol ,triglyceride, total cholesterol & plasma glucose .

Mild hyperuricemia was induced in rats by administration of uricase inhibitor; they became hypertensive by 3 weeks compared to controls which remained normotensive.

Uric acid induces renal vasocontriction mediated by endothelial dysfunction with reduced Nitric acid level and activation of Renin Angiotensin System.

This induces hypertension. In untreated patients with essential hypertension raised uric acid is powerful risks marks for subsequent cardiovascular disease.

Uric Acid stimulates vascular smooth muscle cell proliferation mediated by stimulation of mitogen-activated protein kinase, cyclooxygenase 2, platelet derived growth factor. So elevated uric acid predicts severity of Heart failure and need for heart transplantation in patients with chronic heart failure.

Mild asymptomatic hyperuricemia is associated with decreased renal blood flow, without affecting glomerular filtration rate[78]. Increased renal vascular and systemic hypertensive vascular disease paralleled the raising S.UA levels. These suggest that unexplained hyperuricemia in patients with hypertension most likely reflect early renal vascular involvement[79].Some studies showed raise in UA is associated with renal insufficiency but remain within normal limit in essential hypertension[80] .

The correlation between kidney function & hyperuricemia is present if blood urea was over 30 mg %. Hyperuricemia is present over 1/3 of case of hypertension, while thiazide administration & renal failure increase degree of hyperuricemia. The elevated blood levels are primarily related to disease process itself.

High S. UA & renal failure indicate what was already happened to kidney &does not cause mischief of uric acid. Increased sympathetic out flow alter renal sodium handling by increasing arterial pressure, decreased blood flow and decreased uric acid excretion. This increases S. UA. Raised UA increases purine oxidation and reactive 0xygen species and Angiotensin+ receptor activation. All these, leads to Hypertensive vascular injury.

There is positive correlation between S. UA, cholesterol, triglyceride and index of body size[106]. But, there is negative correlation between White and Blacks whether male or female, but prevalence of HTN was greater in

hyperuricemia compared to normouricemics. Annual increment of S.UA in hypertensive was related to treatment with methyldopa and not related to age, sex, BP control, diuretic therapy or plasma urea.

High S.UA levels were independently associated with proximal tubular sodium reabsorption in men. This relationship suggests an altered tubular sodium handling and uric acid metabolism, consistent with hyperinsulinemia, insulin resistance being the possible pathophysiological link .˙ Hyperurecemia with untreated hypertension was related significantly with alcolhol intake, serum asparate transaminase activity &

obesity.

Elevated childhood S. UA is associated with increased blood pressure beginning in childhood & higher BP levels that persist in adulthood[84,88]. These suggest that Uric acid might have role in early pathogenesis of Essential hypertension[87]. Altered lactic acid metabolism in hypertensive many account for altered renal transport of uric acid. The changes in kidneys are glomerular capillary thickening and sclerosis, tubular atrophy, pigment deposits, degeneration in loops of henle and interstitial deposit of uric acid in renal medullary tissue. Elevated SUA have linked to hypercholesterolemia in normotensive is due to disturbance in lipid metabolism.

S.UA was directly related to BMI, creatinine, triglycericide, LDL cholesterol, components of metabolic syndrome and inversely propotional to

HDL cholesterol. There is significant association of S.UA with preclinical Target organ damage namely LVH, carotid atherosclerosis, microalbuminuria, in untreated essential hypertensive patients. regardless of other cardiovascular risk factors.

In vitro, free uric acid was found to increase vascular smooth muscle cells, monocyte chemoattractant protein I((MCP I),increased mRNA protein expression occurring as early as 3 hrs after uric acid incubation[89].

In addition, UA activated the transcription factors kB, activator protein I, mitogen activated protein kinase signalling molecule ERK p44/42 and p38 and increasedcyclooxygenase 2 mRNA expression.

Hyperuricemia is independent risk factor for CHD, hypertension, hyperlipidemia particularly hypertriglyceridemia than with cholesterol,

Even with treated patients. But recent investigation suggested that relationship between raised uric acid & raised cholesterol is largely mediated through triglyceride and little association between uric acid & HDL cholesterol.

The NHANES 1 Epidemiologic follow study showed raised uric acid level is independently associated with risk of cardio vascularmortality[90]. In Chicago, peoples gas company study showed association between uric acid with prevalence of ECG abnormalities and mortality appeared to be secondary to association between uric acid and other risk factors.

Framingham study showed hyperuricemia is risk factors for CHD even after

correcting for hypertension[92]. However in multivariate analysis including age, systolic BP, relative weight, cigarette smoking and S. Cholesterol, S. Uric acid did not add independently to prediction of CHD. It is linearly related CAD severity is women than in men.

High uric acid is strong independent marker of impaired prognosis with moderate chronic heart failure. There is no relation of S. UA with age, diet, but there is an increase with bodyweight & body mass. Uric acid has direct associated with left ventricular mass index.

Hyperuricemia was strongly associated with metabolic syndrome and also in hypertensive without metabolic syndrome. Uric acid is also strong predictor of stroke with myocardial infarction and non-insulin dependent diabetes mellitus.

Isolated Systolic HTN, Serum creatinine and serum uric acid were predictors of mortality with CVD and stroke.

MATERIALS AND METHODS

PLACE AND DURATION:

The current study is done In Tiruneveli Medical College, Department of Medicine from our inpatient and outpatient departments from August 2013 to August 2014.

INCLUSION CRITERIA:

Group A comprises of 30 healthy individuals aged between 35-65 years. Their BP was recorded < 140/90.

Group B comprises of 30 hypertensive individuals aged between 35-65 years and BP was recorded ≥ 140/90

EXCLUSION CRITERIA:

- Diabetes mellitus
- Ischemic heart disease
- Renal disease
- History and presence of jaundice
- Chronic liver disease
- Familial hyperlipidaemia
- Patients on lipid lowering drugs
- Smoking
- Alcoholics
- Obese BMI <25

- Gout

DATA COLLECTION:

All these subjects in Group A & Group B were conducted a medical examination as per a fixed proforma. Physical examination include following anthropometric measurements.

1) **Height**:

Height was measured by using a vertical board with an attached metric scale. The individual was made to stand bare foot on a flat surface with weight evenly distributed on both the feet, heel together and head positioned so that vision was perpendicular to body. Head, back, buttocks, and heels are in contact with vertical board. The headboard was brought in contact with the head to compress the hair & the reading recorded to the nearest 0.1 cm.

2) **Weight**:

Weight was recorded by making the patient stand on a dial type weighing machine with body weight distributed between both feet.

3) **Body Mass Index** was calculated using formula

Weight in Kg / (Height in meter)2.

- Underweight< 18
- Normal – 18-24.9
- Grade I (over weight) -- 25-29.9
- Grade II (obese) – 30-39.9

- Grade III (very obese) > 40

4) METHOD OF RECORDING BLOOD PRESSURE:

Instrument used is sphygmomanometer. It is kept level of heart and cuff tied around upper arm. Systolic pressure is first measured by palpatory method and then pressure is raised to 20 mm above the measured systolic pressure & then of gradually released. Variation of sound was heard with stethoscope placing its chest piece on brachial artery, a little below the cuff. The sounds are heard due to occurrence of turbulence in flow of blood through the narrow blood vessel, when the manometric pressure just coincides with systolic blood pressure.

When pressure from cuff is released, normal stream line flow sets in & sound is no longer heard. This manometric pressure coincides with diastolic Blood pressure. As pressure is released, various sounds are heard known as Korokoff sounds.

- Phase I-sudden appearance of tapping round persist for 15 mmHg. This indicates systolic pressure.
- Phase II – murmur persist for another 15 mm Hg.
- Phase III – clear loud gong sound for 20mm Hg.
- Phase IV – muffled & fading sound. This indicate diastolic pressure.

BP is recorded 3 times at 30 min interval and mean BP is taken.

BIOCHEMICAL TESTS:

Morning sample blood was drawn after 12 hrs fasting. The samples of blood were allowed to stand to clot. Precautions were taken so that the blood did not haemolyse. Serum was separated by centrifugation. and analysed by the following methods.

METHODOLOGY:

Calorimetric, enzymatic method with glycerophospate oxidase. This reagent is based on the method of wako and the modifications by Mc Gowan et al and Fossati et all.

PRINCIPLE:

Triglycerides +H_2O →glycerol + free fatty acids

Glycerol + ATP → Glycerol 3 phosphate + ADP

Glycerol 3 phosphate + O_2→ DAP + H_2O_2

H_2O2 + 4AAP +3,5DHBS → Quinoneimine dye + $2H_2O$

The intensity of quinoneimine formed is proportional to the triglycerides concentration in the sample when measured at 505 nm(500-540nm)

PROCEDURE:

Pippette in tubes marked	blank	Standard	Test
Working reagent	1000 ul	1000ul	1000ul
Distilled water	10ul	-	-
Standard	-	10ul	-
Sample	-	-	10ul

Mix and incubate for 10 minutes at 37 degree c, read the absorbance of standard and each sample at 505/670 nm on biochromatic analysers against reagent blank.

CALCULATION:

Triglycerides (mg/dl) = abs of test/abs of standard * concentration of std (mg/dl).

CHOLESTEROL:

METHODOLOGY:

The method is based on the Trinders methodology

PRINCIPLE:

Cholesterol ester + H_2O → Cholesterol + fatty acids

Cholesterol + O_2→ Cholest-4-en-3-one + H_2O_2

$2H_2O_2$ + 4AAP + Phenol → Quinoneimine dye + $4H_2O$

Absorbance of Quinoneimine so formed is directly proportional to cholesterol concentration.

PROCEDURE:

Pippette in tubes marked	blank	Standard	Test
Working reagent	1000 ul	1000ul	1000ul
Distilled water	10ul	-	-
Standard	-	10ul	-
Sample	-	-	10ul

Mix well and incubate for 5 minutes at 37 degree c or 10 minutes at 20 -25 degree c. read the absorbance of the test and standard against reagent blank.

CALCULATION:

Cholesterol (mg/dl) = abs of test/abs of standard * concentration of std (mg/dl).

HDL DIRECT:

The assay is based on a modified polyvinyl sulfonic acid and polyethylene glycol methyl ether coupled classic precipitation method with the improvements in using optimised quantities of PVS/PEGME and selected detergents. LDL, VLDL and chylomicron react with PVS and PEGME and the reaction results in the inaccessibility of LDL, VLDL and chylomicron by cholesterol oxidase and cholesterol esterase. The enzymes selectively react with HDL to produce H_2O_2 which is detected through a

trinder reaction.

HDL + LDL+VLDL+CM → HDL +(LDL+VLDL+CM) + PVS/PEGME

HDL → fatty acid + H_2O_2

$2H_2O_2$ + 4-AA +TODB → Quinone +$5H_2O$

SERUM URIC ACID:

METHODOLOGY:

The reagent is based on trinders reaction, enzymatic and colorimetric method.

PRINCIPLE :

Uric acid + O_2 +H_2O → ALLANTOIN + CO_2 + H_2O_2

TOOS + 4AAP + $2H_2O_2$→ Quinoneimine dye + $4H_2O$

The intensity of colour formed is proportional to the uric acid concentration.

PROCEDURE:

Pippette in tubes marked	blank	Standard	Test
Working reagent	1000 ul	1000ul	1000ul
Distilled water	10ul	-	-
Standard	-	10ul	-
Sample	-	-	10ul

Mix and incubate for 5 minutes at 37 degree c, read the absorbance 546/670 nm on barometric analysers against reagent blank.

CALCULATIONS:

Uric acid = abs of test/abs of standard * concentration of std (mg/dl).

VLDL = Triglyceride/ 5

LDL = Total cholesterol – (HDL +VLDL) by Freidewelds formula

OBSEVATION &RESULTS

STATISTICAL ANALYSIS

STUDY DESIGN

A Case –control study consisting of 30 controls and 30 cases is undertaken to study the relationship between serum uric acid and lipid parameters

STATISTICAL ANALYSIS

The information collected regarding all the selected cases were recorded in a Master Chart.

The range, frequencies, percentages, means, standard deviations, chi square, ‘t’ value and 'p' values were calculated.

Student’s ‘t’ test was used to test the significance of difference between quantitative variables .

Yate’s and Fisher’s chi square tests for qualitative variables.

A 'p' value less than 0.05 is taken to denote significant relationship.

SIGNIFICANT FIGURES: P VALUE

Suggestive significance $0.05<P<0.10$

Moderately significant $0.01<P \leq 0.05$

Strongly significant $P \leq 0.01$

RESULTS:

TABLE 8: AGE DISTRIBUTION

Age Group	Hypertensive Group		Control Group	
	No	**%**	**No**	**%**
35 – 45 yrs	8	26.7	9	30
46 – 55 yrs	10	33.3	12	40
56 – 65 yrs	12	40	9	30
Total	**30**	**100**	**30**	**100**
Range	36 – 64 yrs		36 – 64 yrs	
Mean	50.8 yrs		50.4 yrs	
SD	8.5 yrs		8.6 yrs	
'p'	0.88 Not Significant			

The individuals selected for both cases and controls are categorized age wise and stratified into three age categories and looked for any specific increase in the blood pressure, serum lipid profile and serum uric acid.

Using the table it is calculated that the mean age of hypertensive cases is about 50.8 years and in controls it is about 50.4 years.

The distribution of cases and controls is equal among different age groups

All cases have blood pressure > 140/90 mmhg

All controls have blood pressure <140/90mmhg

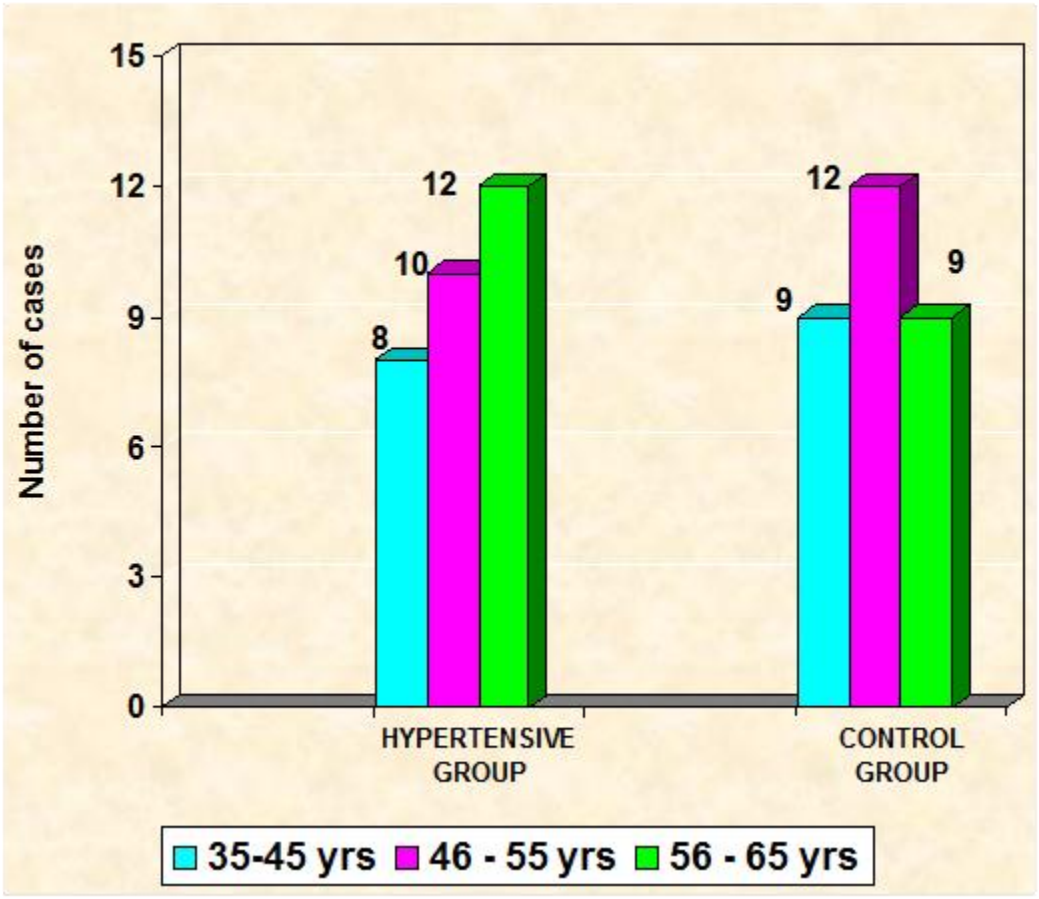
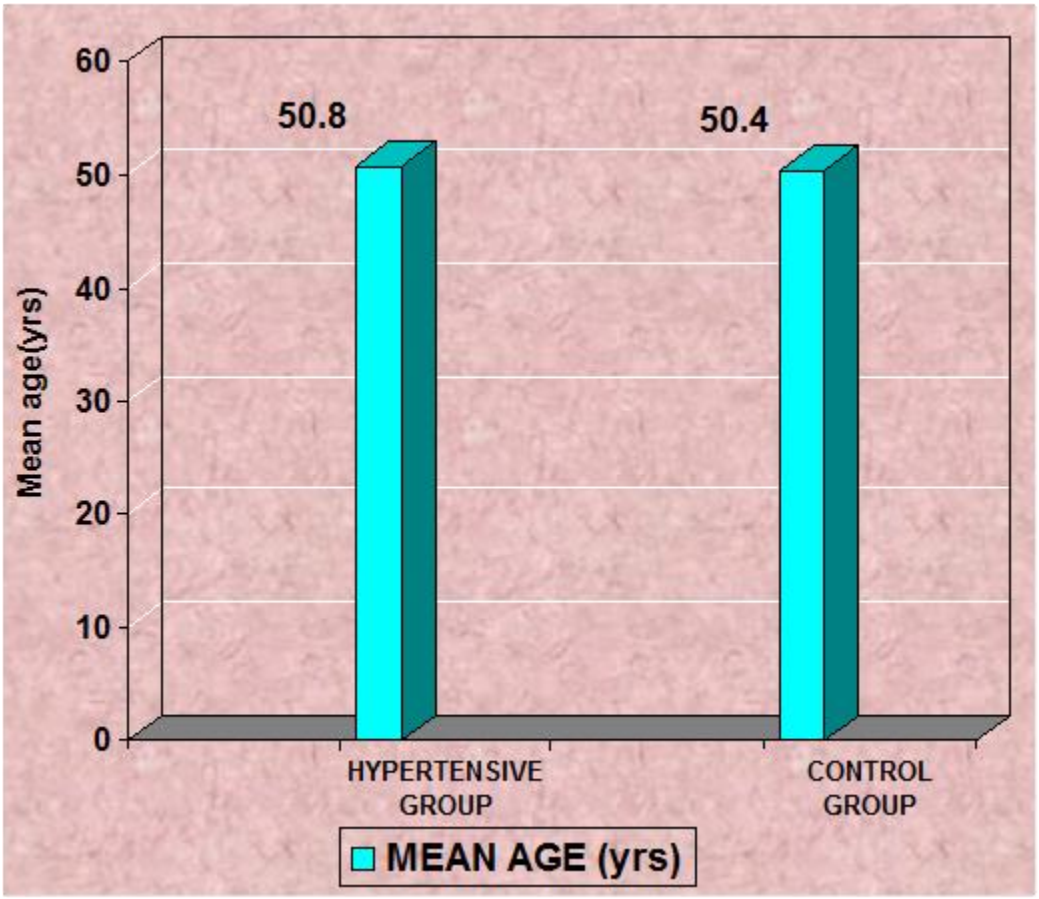


FIGURE 9: AGE DISTRIBUTION IN HYPERTENSIVE CASES



.**FIGURE 10 : Mean age in hypertensive and control group**

So the number of hypertensive were more in the age group of 55to 65 years in comparison with the age in the hypertensive cases**.**

The mean age in the hypertension group is calculated about 50.8 years. The distribution of cases and controls is equal between controls and cases and so the 'p' value is statistically not significant.

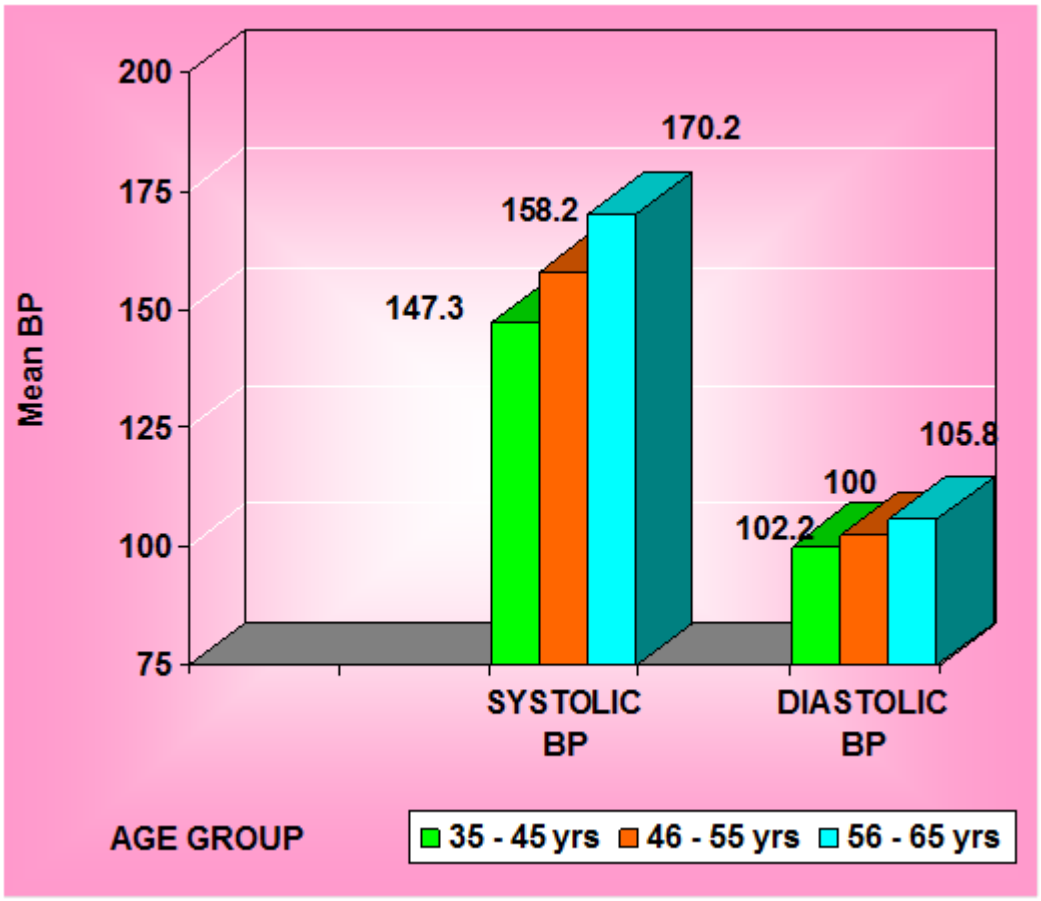


FIGURE 11: Age group wise blood pressure elevation

The diagram shows the age wise elevation of blood pressure.

Of the hypertensive population, elevation of blood pressure is higher in the age group of 55 to 65 years, since arteriosclerosis and vascular changes contribute more to them.

TABLE 9: AGE GROUP AND BLOOD PRESSURE ELEVATION

Age Group	Blood pressure in Hypertensive group			
	Systolic B.P.		Diastolic B.P.	
	Mean	SD	Mean	SD
35 - 45	147.3	2.4	100.0	0.0
46 – 55	158.2	6.0	102.2	4.2
56 - 65	170.2	4.0	105.8	5.3
‘p’	<0. 0001 Significant		0.0133 Significant	

The table shows blood pressure elevation is seen more in the age group of 55 to 65 years.

‘P’ value is significant indicating that there is a significant correlation relating the age group and blood pressure elevation.

Both systolic blood pressure and diastolic pressure tend to show correlation with the age group.

‘P’ value is significant in both hypertensive and control population.

TABLE 10: SEX DISTRIBUTION

Group	Sex			
	Male		Female	
	No	%	No	%
Hypertensive	15	50	15	50
Control	15	50	15	50
'p'	1.0 Non Significant			

The sex distribution is equal between cases and controls.

Both in hypertensive cases and also in the controls, both men and women were equally distributed for an effective and comparison.

The table shows that the 'p' value calculated is statistically not significant.

FIGURE 12: Sex distribution in hypertensive and control

The bar diagram shows there is an equal distribution sex both in case and control population.

BMI, HEIGHT AND WEIGHT IN STUDY POPULATION

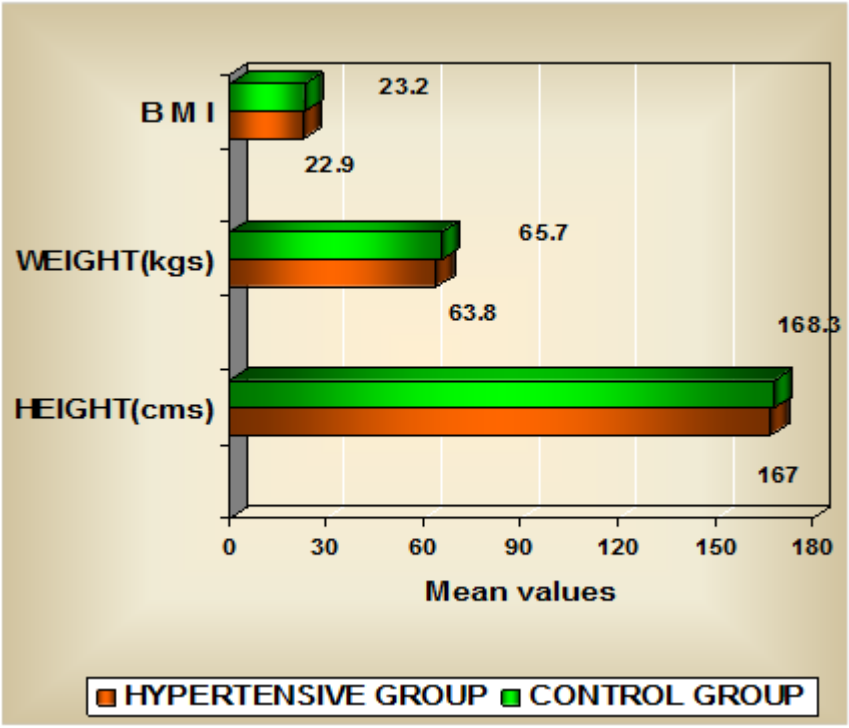


FIGURE 13: BMI, Height, and Weight in study population

The heights, weight of the individuals were measured and BMI calculated and obese individuals were excluded from the study by the fixed criteria.

The mean values calculated for both hypertensive cases and controls were shown in the diagram.

The mean BMI for hypertensive cases is 23.2 and for cases it is 22.9.

PULSE RATE:

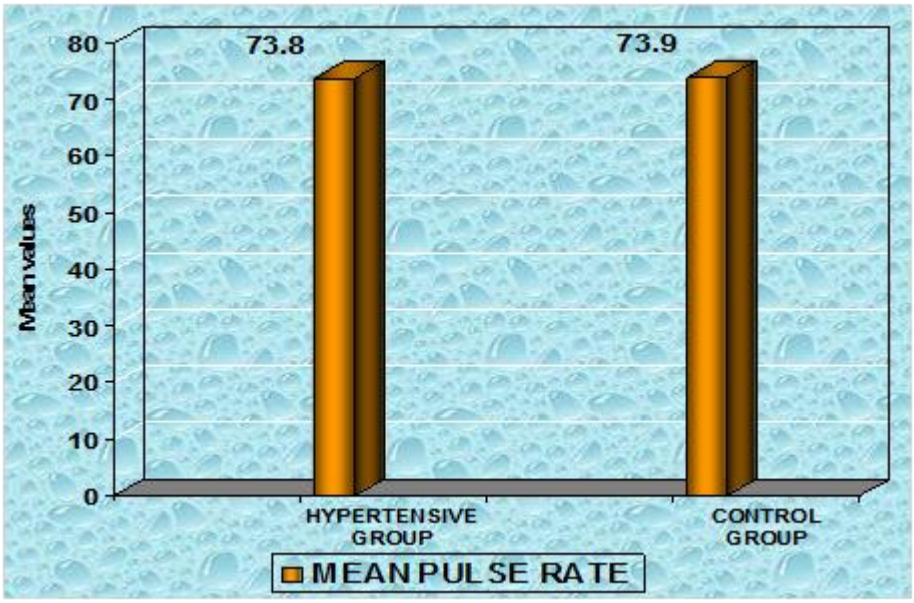


FIGURE14: Mean pulse rate in hypertensive and controls

The pulse rate measured for both the hypertensive cases and in the control group was found to be in normal range with no variation.

TABLE 11: BLOOD PRESSURE

Group	Systolic B.P			Diastolic B.P		
	Range	**Mean**	**SD**	**Range**	**Mean**	**SD**
Hypertensive	144 - 178	160.1	10.4	96 – 112	103.1	4.7
Control	110 - 130	120.1	7.6	78 – 84	80.1	0.9
'p'	**<0.0001 Significant**			**<0.0001 Significant**		

The blood pressure for both the hypertensive cases and controls were plotted and mean blood pressure for both the study population obtained.

All the hypertensive cases have blood pressure > 140/90mmhg.

All the controls have blood pressure <140/90mmhg

SYSTOLIC AND DIASTOLIC BLOOD PRESSURE IN STUDY POPULATION

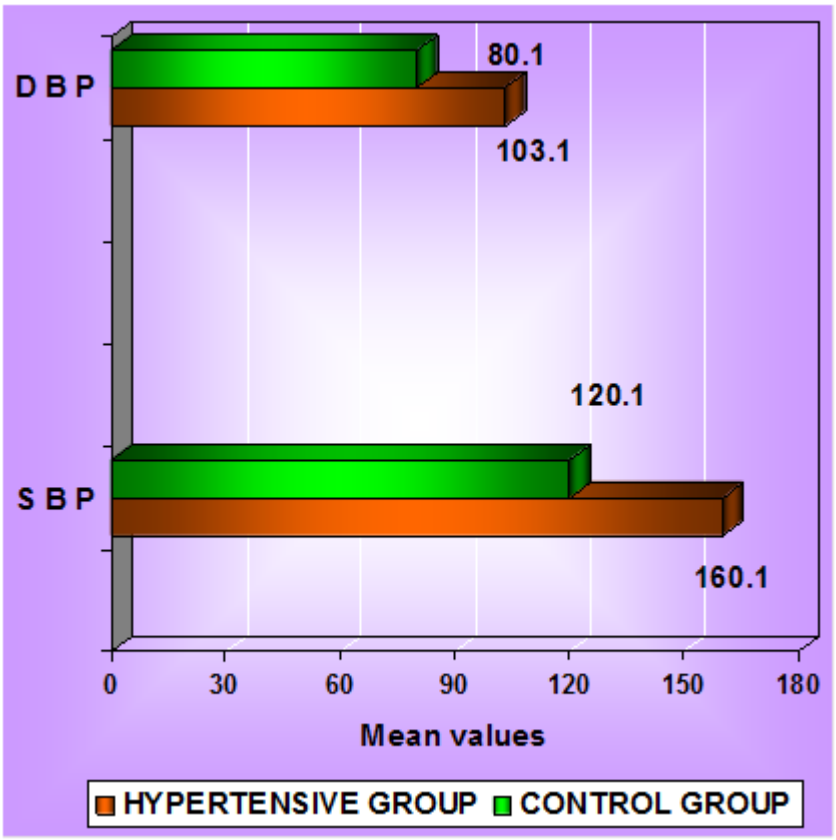


FIGURE15: Mean systolic and diastolic bp in study population

The mean systolic and diastolic blood pressure measure in the hypertensive cases is about 160 and 103 respectively.

DYSLIPIDEMIA

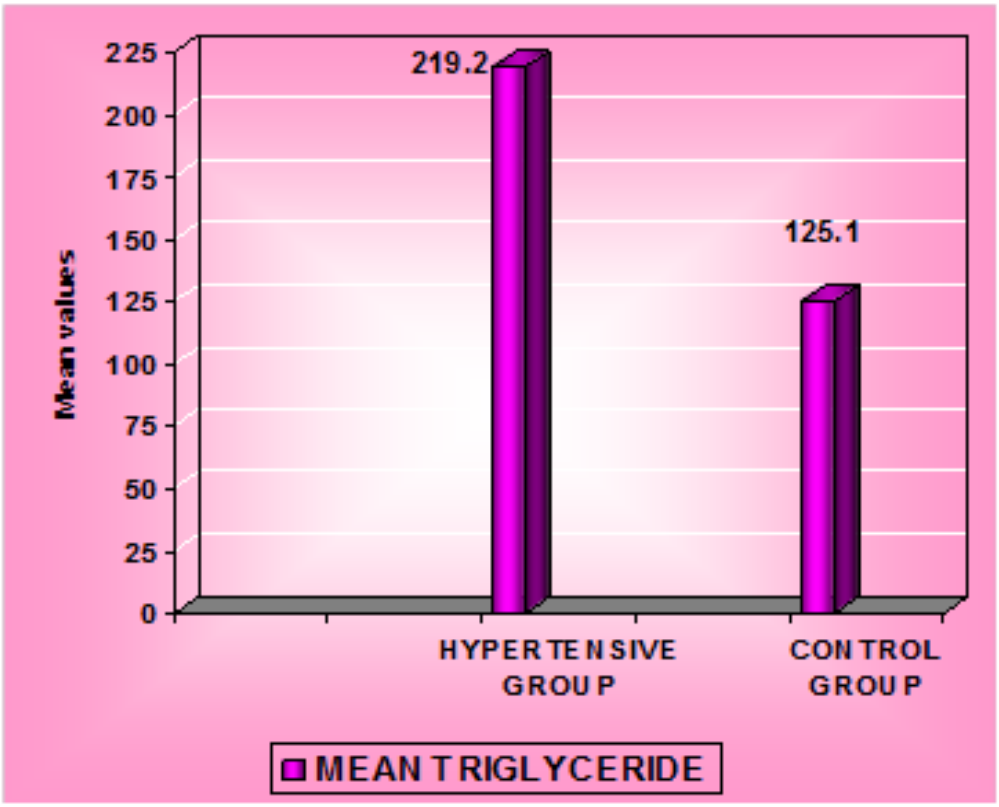
TABLE12: TRIGLYCERIDE

Group	Triglyceride						
	Normal		Abnormal		Range	Mean	SD
	No	%	No	%			
Hypertensive	8	26.7	22	73.3	118 - 294	219.2	42.3
Control	27	90	3	10	78 - 224	125.1	39.1
'p'	**<0.0001 Significant**						

The triglyceride levels were found to be elevated in hypertensive cases, when compared to controls.

The 'p' value is <.001, which is significant denoting the correlation in hypertensive cases, when compared to controls.

FIGURE16: Mean triglyceride levels



The mean triglyceride level found in hypertensive cases is 219.2. In control population, the mean value is 125.

TABLE 13: TOTAL CHOLESTEROL

Group	Total Cholesterol						
	Normal		Abnormal		Range	Mean	SD
	No	%	No	%			
Hypertensive	7	23.3	23	76.7	180 – 316	249.7	42.0
Control	28	93.3	2	6.7	120 – 224	160.1	25.3
'p'	**<0.0001 Significant**						

The total cholesterol values were also observed to be elevated in hypertensive cases.

In control population, only few individuals have elevated total cholesterol values.

The 'p' value is<.001 which is significant correlating the relation in hypertensive cases, when compared to controls.

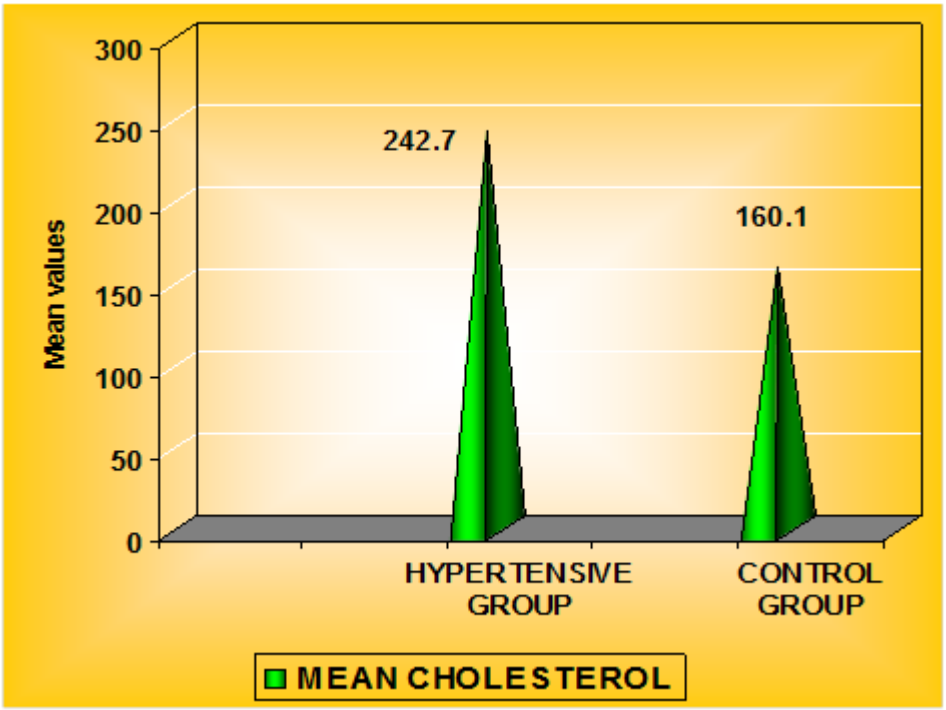


FIGURE 17: Mean cholesterol values.

The mean total cholesterol value in hypertensive is 242 mg/dl and in controls, it is 160mg/dl.

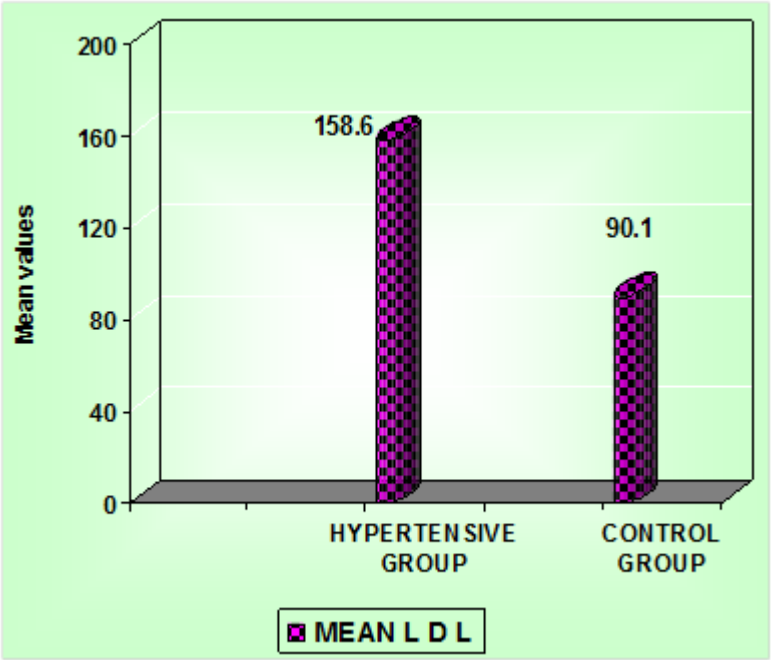
TABLE14: LDL

Group	LDL						
	Normal		Abnormal		Range	Mean	SD
	No	%	No	%			
Hypertensive	9	30	21	70	48 - 259	158.6	50.2
Control	28	93.3	2	6.7	50 - 180	90.1	28.5
'p'	**<0.0001 Significant**						

The LDL levels were elevated in hypertensive group, when compared to control population.

The 'p' value is <.0001, which is significant showing the correlation of elevated LDL level in hypertensive population.

FIGURE18: Mean LDL levels



The mean LDL level in hypertensive cases is 158

And in control group, the mean value is 90.

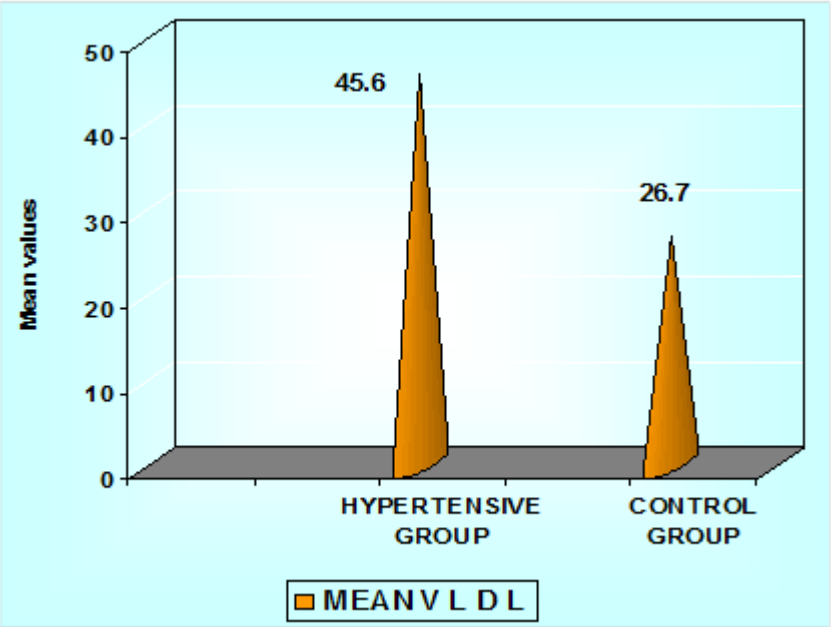
TABLE15: VLDL

Group	VLDL						
	Normal		Abnormal		Range	Mean	SD
	No	%	No	%			
Hypertensive	10	33.3	20	66.7	28 - 65	45.6	8.6
Control	27	90	3	10	14 - 50	26.7	8.8
'p'	**<0.0001 Significant**						

The VLDL levels were elevated in hypertensive cases in comparison with the control population.

The 'P' value is <0.0001, which is statistically significant showing the elevation of VLDL levels in hypertensive population.

FIGURE 19: MEANVLDL LEVELS



The mean VLDL in hypertensive cases is 45.6.

And in control group, it is 26.7.

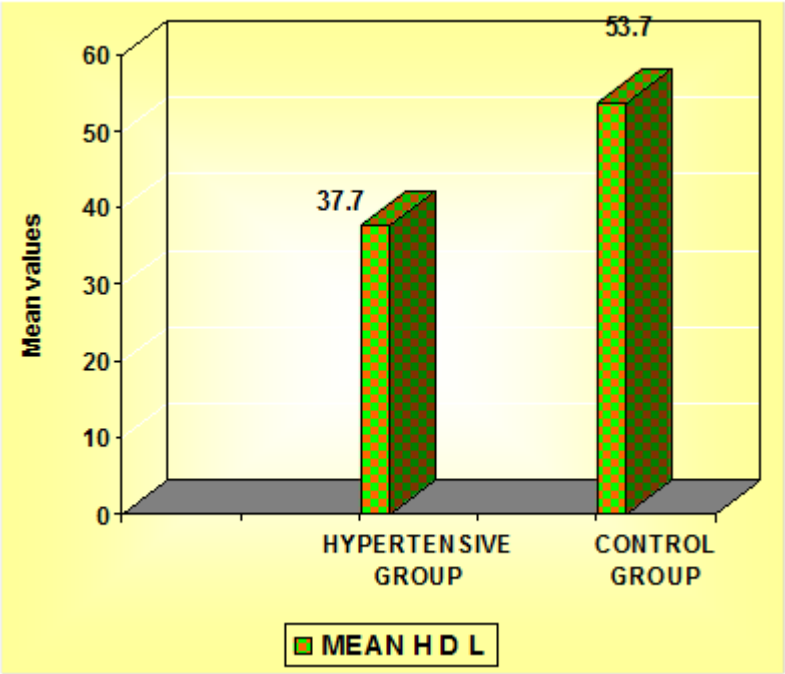
TABLE 16: HDL

Group	HDL						
	Normal		Abnormal		Range	Mean	SD
	No	%	No	%			
Hypertensive	12	40	18	60	23 - 68	37.7	9.6
Control	29	96.7	1	3.3	36 - 80	53.7	10.5
'p'	**<0.0001 Significant**						

The HDL levels were observed to be decreased in hypertensive population, when compared to controls.

The 'P' value is<.0001, which is statistically significant showing the correlation of decreased levels of HDL in hypertensive population.

FIGURE 20: Mean HDL levels



The mean value of HDL in hypertensive cases is 37.7

And in control group, it is 53.7.

TABLE 17: DYSLIPIDAEMIA

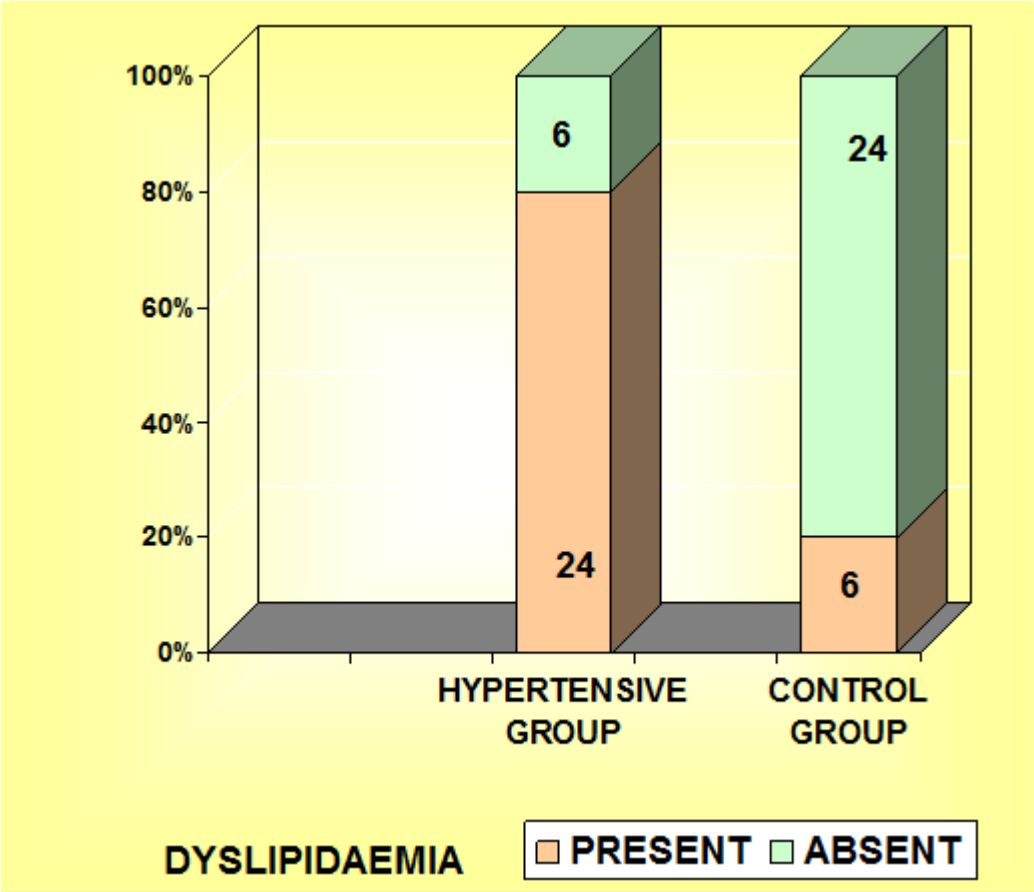
Group	Dyslipidaemia			
	Present		Absent	
	No	%	No	%
Hypertensive	24	80	6	20
Control	7	23.3	23	76.7
'p'	<0.0001 Significant			

The lipid parameters as a whole, or as an individual parameter elevation is seen mostly in hypertensive cases, when compared with controls.

The 'P' value is statistically significant showing the correlation of elevation in hypertensive population when matched with the control population

DYSLIPEDEMIA

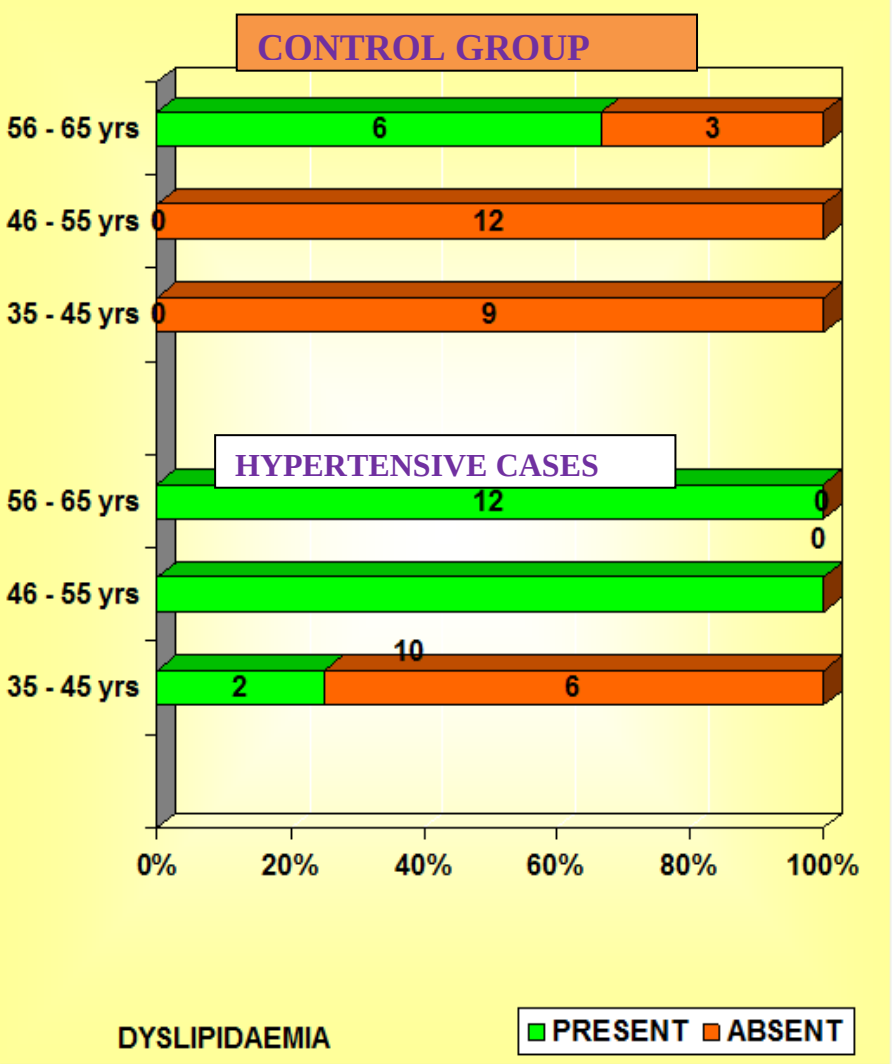
FIGURE 21: Dyslipidemia in hypertensive and control group



The elevation of triglyceride, total cholesterol, LDL,VLDL or as an individual parameter elevation is seen about 24 individuals in hypertensive cases, where as in the control population it is only about 6 cases , mostly of which is elevated triglyceride levels.

This clearly shows that the hypertensive population has been associated with the elevation of lipid parameters, in comparison with the control population.

FIGURE 22: Age and dyslipedemia



In the hypertensive population, more occurrence of dyslipidemia is seen in the age group of 55 to 65 years.

Since the severity of BP elevation is more in age group 55 to 65 year age group, dyslipidemia is more seen in the age group 55 to 65 year age group.

Thus it also implies that dyslipidemia is also related with severity of elevation of BP and it can also be age related.

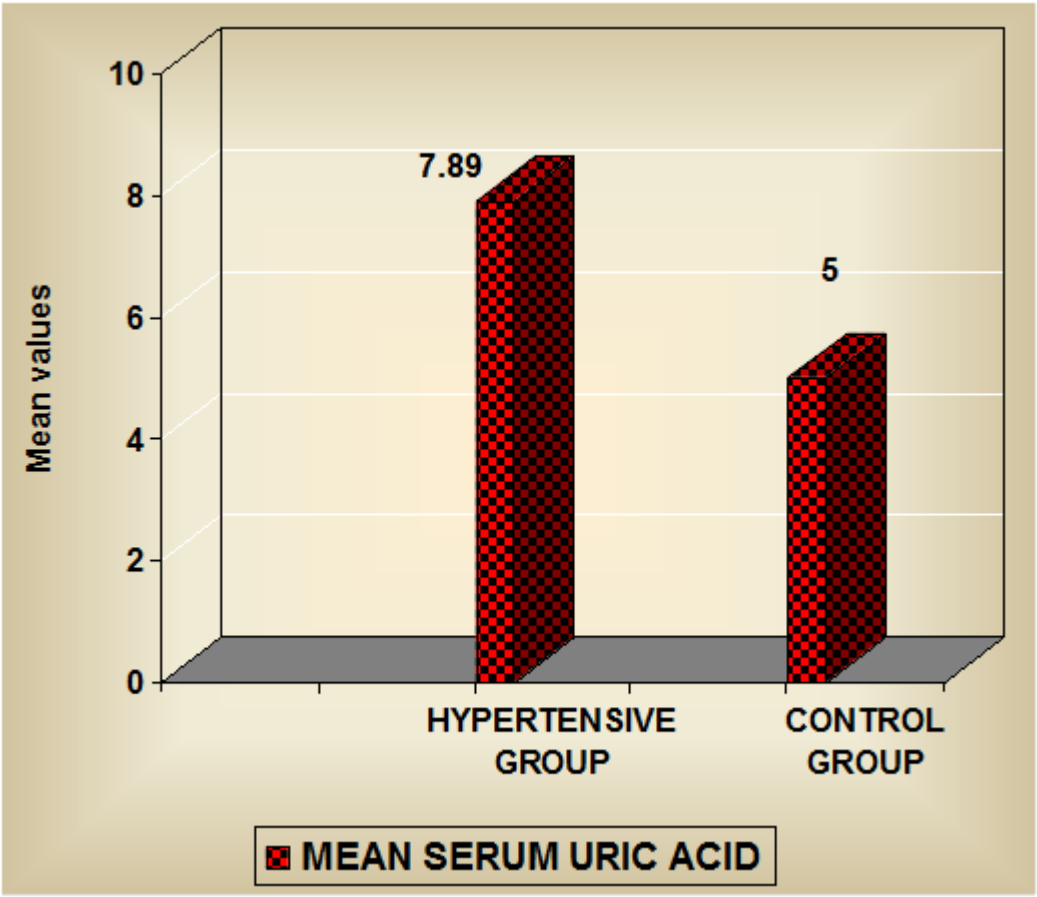
TABLE 18: SERUM URIC ACID

Group	Serum Uric Acid						
	Normal		Abnormal		Range	Mean	SD
	No	%	No	%			
Hypertensive	5	16.7	25	83.3	6.3 – 9.8	7.89	0.91
Control	30	100	-	-	4.2 – 5.6	5.0	0.44
'p'	**<0.0001 Significant**						

Serum uric acid levels are observed to be elevated in most of the hypertensive population, where as in control population, no elevation of uric acid is observed.

25 cases of hypertensive cases have found to be increased levels of uric acid from its normal value.

FIGURE23: Mean serum uric acid level



The serum uric acid levels found to be elevated in most of the hypertensive cases in comparison to the control population.

This clearly depicts the correlation of elevation of serum uric acid with hypertension. In control population, no uric acid elevation is seen.

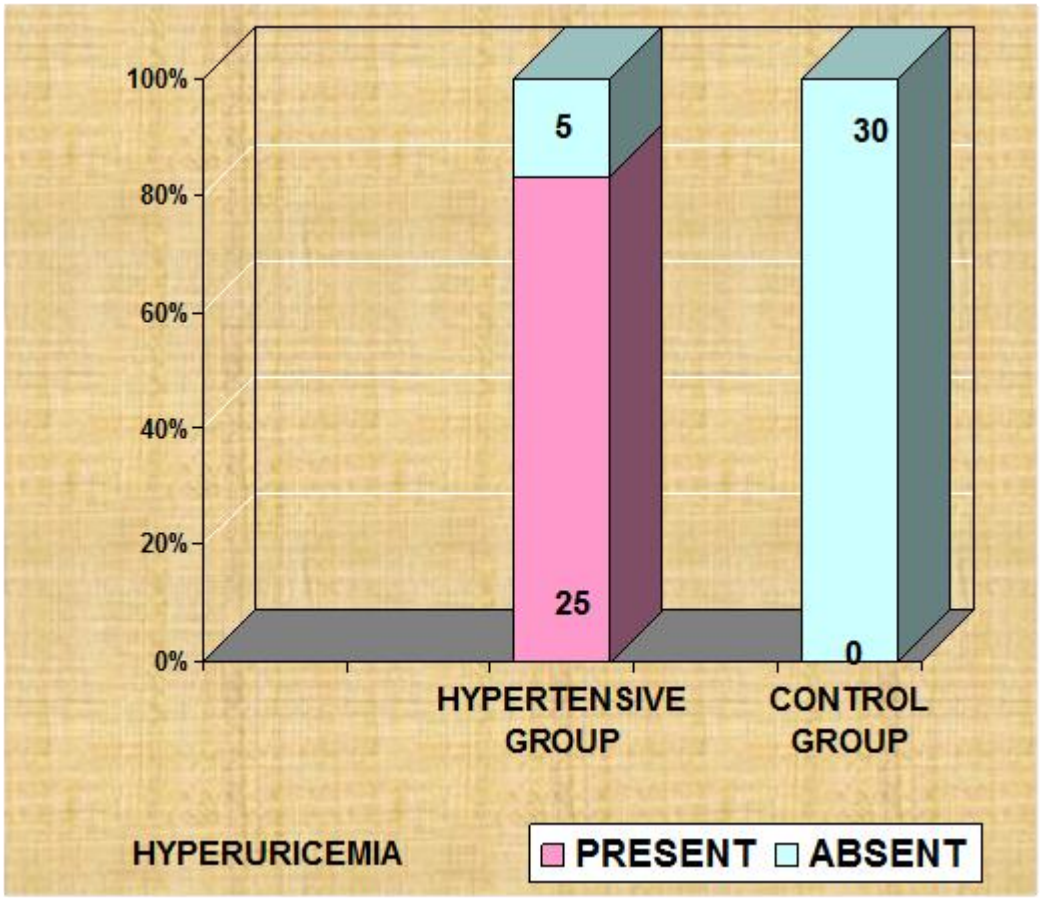
TABLE19: HYPERURICEMIA

Group	Hyperuricemia			
	Present		Absent	
	No	%	No	%
Hypertensive	25	83.3	5	16.7
Control	-	-	30	100
'p'	<0.0001 Significant			

In hypertensive cases, 25 cases have shown elevation of serum uric acid, and no controls have shown the elevation of uric acid.

In hypertensive cases, 'P' value is significant denoting the vital correlation between the elevation of uric acid in hypertensive population.

FIGURE24: Hyperuricemia



FIGURE

This diagram shows the number of hypertensive individuals showing the elevation of uric acid.

The control group does not show any elevation of uric acid.

BLOOD GLUCOSE:

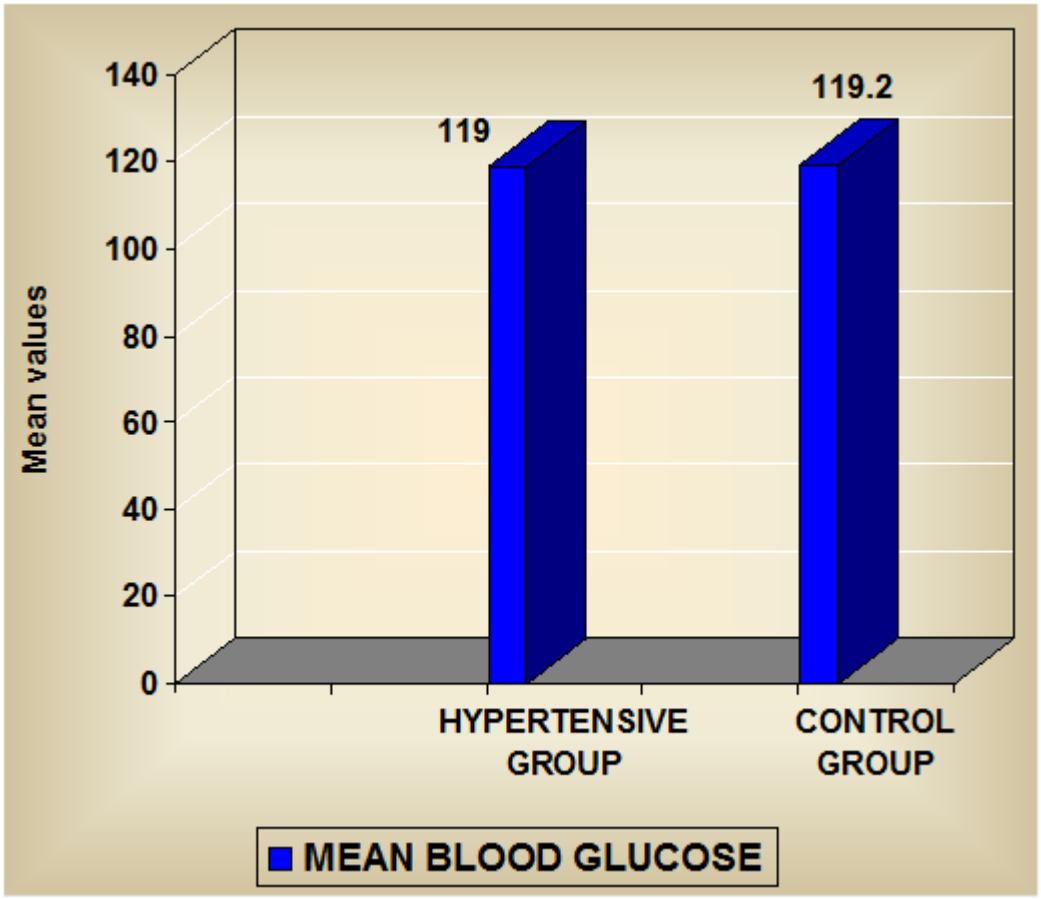


FIGURE25: Mean blood glucose level

Diabetic patients have been excluded from the study population .The diagram shows normal value of blood sugar in both hypertensive and control population

SERUM UREA AND CREATININE:

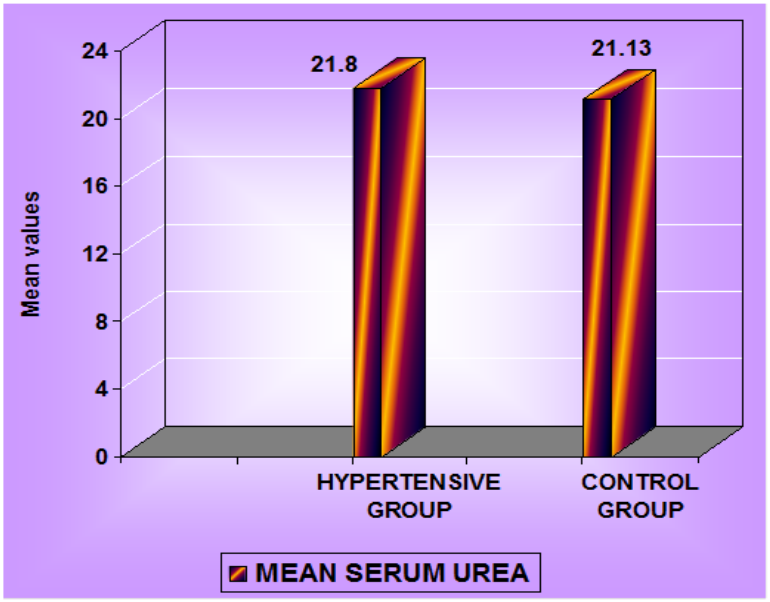


FIGURE 26: Mean serum urea level

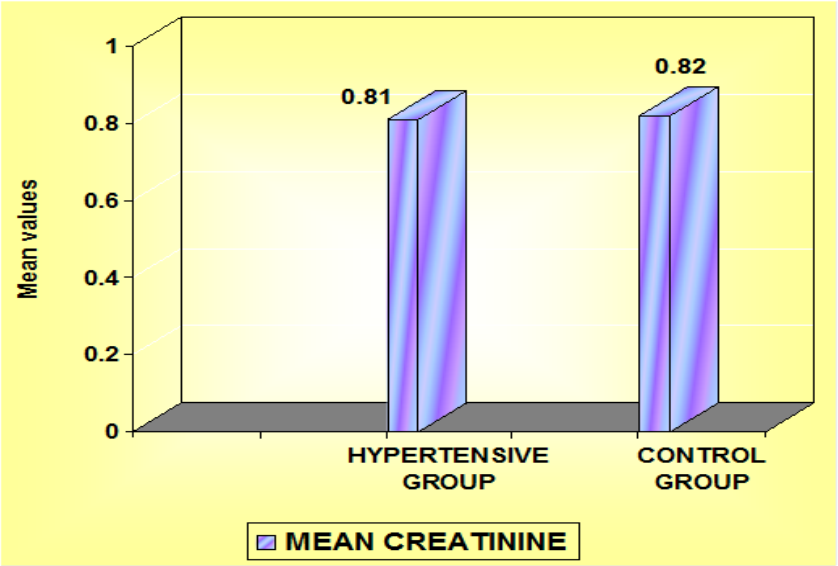


FIGURE 27: Mean serum creatinine level

Renal disease is excluded from the study population.

Serum urea and creatinine values are normal both in hypertensive cases and control population

TABLE 20: DYSLIPIDAEMIA AND HYPERURICEMIA

Dyslipidaemia	Hypertensive Group				Controls Group			
	Hyperuricemia				Hyperuricemia			
	Present		Absent		Present		Absent	
	No	%	No	%	No	%	No	%
Present	24	100	-	-	-	-	7	100
Absent	1	16.7	5	83.3	-	-	23	100
'p'	**<0.0001 Significant**				--			

In the hypertensive group, most of the individuals, about 80% have dyslipidemia and are associated with increased level of serum uric acid.

In the control population, dyslipidemia is seen only in around 20% of population and in them also, serum uric acid level is not elevated.

The 'P' value is significant implying the correlation of relationship between serum uric acid and dyslipdemia in hypertensive cases, where as in controls no such relation is seen.

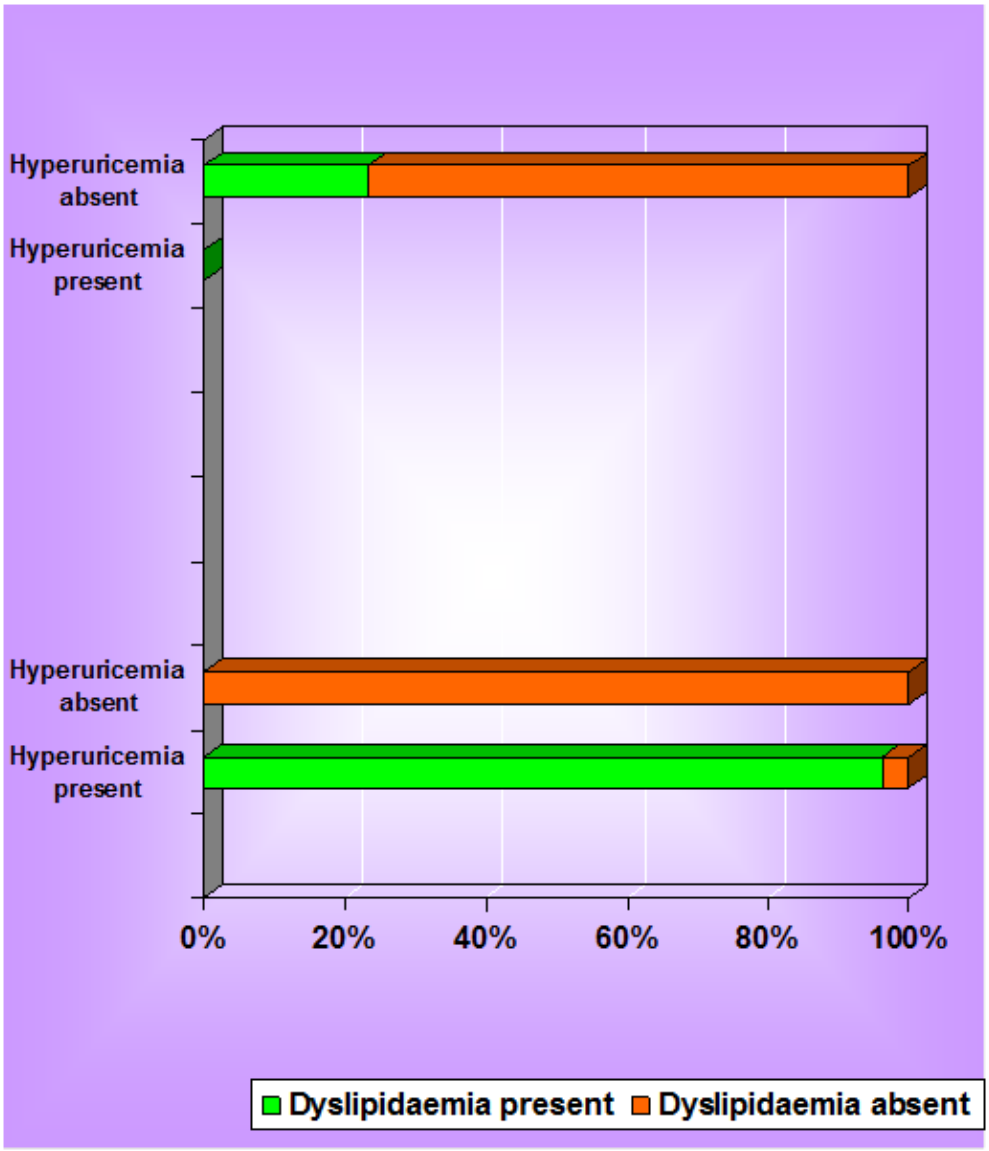


FIGURE 28: Dyslipedemia and hyperuricemia

In hypertensive population, most of the individual have dyslipidemia and they are associated with elevation in serum uric acid.

Even elevation in any one of the lipid parameter is associated with elevation in serum uric acid. In control population, only few of them has dyslipedemia and in them also, no elevation of serum uric acid is observed.

This demonstrates the correlation of dyslipidemia and uric acid in essential hypertension

DISCUSSION

1. AGE AND BLOOD PRESSURE ELEVATION

Blood pressure elevation is observed as the age group increases. As age increases, a rise in blood pressure elevation is observed.

The level of blood pressure rise is observed more in 55-65 year age group.

Also more number of hypertensive are observed in 55-65 age group.

Blood pressure rises with age and this rise is observed more in age group 55-65 years age group and this shows the blood pressure elevation is associated with rise in age group.

TABLE 8, 9 shows the relation between age group and hypertension.

FIGURE 9,10,11 age distribution in hypertensive cases, mean age in hypertensive and control group and age group wise blood pressure elevation respectively.

2. DYSLIPIDEMIA AND HYPERTENSION

An elevated level of triglycerides, LDL, VLDL and decreased level of HDL is observed more in hypertensive group. Most of the individuals in hypertensive group has elevation of lipid parameters as a whole or rise in any one of the individual lipid parameter, excluding HDL.

About 24 out of 30 cases in the hypertensive group has observed to have dyslipidemia ,either as total increase in all lipid parameters or increase in any one of the lipid parameter ,excluding HDL.

In control population only few of the individuals have dyslipidemia, most of the control population do not have any lipid abnormality. Only 4 of 30 have increased triglycerides and 2 of them have increased cholesterol levels .

So, about 80% of hypertensive population have dyslipidemia.

In control population, only 20% have dyslipidemia and they too have only increased triglyceride levels.

Also the rise in lipid parameters is more with age group, more seen in 55-65 years age group and the elevation also increases with increase in blood pressure.

The proportion and also magnitude of dyslipedemia both increases with age and blood pressure

This implies that dyslipedemia shows a direct relationship with both increase in age and has correlation with elevation in blood pressure.

TABLE 12,13,14,15 shows the ‘P’ value is statistically significant denoting the correlation of rise of triglyceride, total cholesterol, LDL, VLDL with hypertension.

FIGURE 16,17,18,19 shows mean triglyceride, cholesterol, LDL, VLDL levels in both study population and it is observed that there is an elevation of triglyceride, cholesterol, LDL, VLDL in hypertensive group, when compared with control population.

TABLE 16 shows the ‘P’ value is statistically significant showing the decrease in HDL is significant in essential hypertensive.

FIGURE 20 shows the observed decreased mean HDL levels in hypertensive group compared to control group.

TABLE 17 shows most individuals in hypertensive group have dyslipidemia, compared to controls who have only few individuals with triglyceride elevation.

FIGURE 21 shows 80 % of hypertensive group have dyslipidemia and 20% of control population have triglyceredemia.

3. SERUM URIC ACID AND HYPERTENSION:

Uric acid elevation is seen in most of the individuals in hypertensive group. About 25 of 30 people have elevation of serum uric acid and its

elevation is directly proportional to rise in blood pressure. This implies that serum uric acid level is an independent risk factor in hypertension and its level also correlates with the severity of hypertension.

Uric acid level is not elevated in control group.

This shows that uric acid elevation is seen in hypertensive group and not in control.

TABLE 18 shows ‘P’ value is statistically significant denoting the correlation of elevation of serum uric acid in essential hypertension.

FIGURE 23 shows serum uric acid elevation in hypertensive group, where as in control population serum uric acid is not elevated.

TABLE 20 shows ‘P’ value is statistically significant denoting the correlation of elevation of serum uric acid with dyslipidemia.

FIGURE 28 shows the elevation of serum uric acid in hypertensive group with dyslipidemia, where as in controls even with dyslipidemia ,serum uric acid is not elevated.

4 .DYSLIPEDEMIA AND URIC ACID ELEVATION:

Dyslipedemia is seen in most of the hypertensive cases. About 24 out of 30 cases has elevation in lipid parameters. About 80% of study population have elevated dyslipidemia observed.

In all hypertensive individuals with elevated lipid parameters, it is observed that the serum uric acid level is elevated. The serum uric acid elevates, either with rise in all of lipid parameters or if any one of the lipid parameter is elevated, excluding HDL.

The rise in serum uric acid is also proportional to the severity of hypertension and also with the age group.

In control population, serum uric acid level is not elevated.

In control population, only few have dyslipidemia. About 6 of 30 individuals have dyslipidemia and they too have elevated triglycerides and total cholesterol values alone. Even in those individual with dyslipidemia, serum uric acid level is not elevated.

This implies that dyslipidemia is associated with elevation of serum uric acid in hypertensive group, where as in control group dyslipedemia is not associated with elevation of serum uric acid.

This clearly denotes the correlation of serum uric acid and dyslipidemia in essential hypertension

Dyslipidaemia in hypertension is due to lipid deposition in lumen of arterial wall, causing atherosclerosis. This increases the resistance to flow of blood in blood vessel, causing hypertension. HDL-Cholesterol impairs endothelium dependent dilation. HDL-cholesterol is a protective factor

decreased in hypertensive, suggesting more risk of developing complication of hypercholesterolemia[92]. High cholesterol influence adrenergic stimulation and outcome of target organ damage is more in hypertensive.

LDL-cholesterol is vasoconstrictor, mitogenic, proinflammatory and thrombogenic. So its raise in hypertensive is a risk for developing complications.

Hypertension is a degenerative process, taking place in blood vessels affecting blood supply to target organs like Heart, Kidney and Liver. Damage to these organs is called Target Organ Damage[108]. These degenerative process increases purine metabolism also, rising uric acid levels.

In hypertension, there is enhanced proximal tubular reabsorbtion and depressed tubular secretion of uric acid causing hyperuricemia. Diuretic treatment of hypertension will also cause hyperuricemia. Hyperuricemia is present in 1/3 rd cases of hypertension and increased in thiazide treatment.

Uric acid is an independent risk factor for atherosclerosis. . Uric acid excretion is affected by kidney due to decreased renal perfusion in hypertension.

Hypertension complication like CCF, Heart failure has more endothelial dysfunction due to dyslipidaemia and raised uric acid.

So in all hypertensive, dyslipidaemia and serum uric acid is correlated. Detection of this correlation at an early stage will prevent complications of hypertension.

CONCLUSION

Dyslipidemia is seen in essential hypertensive individuals.

Elevation of triglycerides, rise in total cholesterol, raised LDL and raised VLDL is observed in Essential hypertensive individuals. The levels of HDL are observed to be low in Essential hypertensive individuals.

Elevation of serum uric acid level is seen in essential hypertensive. Both dyslipidaemia and hyperuricemia observed to be elevated with increase in age in essential hypertensive.

In normotensives, few have elevated triglyceride levels and elevated total cholesterol levels. Though hypertriglyceridemia increase as age increase, it is not associated with hyperuricemia.

This concludes that dyslipidaemia is correlated to hyperuricemia in essential hypertensive and not in normotensive.

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ANNEXURES

ANNEXURE - I

A PROSPECTIVE STUDY OF CORRELATION BETWEEN SERUM URIC ACID AND DYSLIPIDEMIA IN ESSENTIAL HYPERTENSION

PROFORMA

Case No: **Date :**

Name of the patient:

Age:

Sex:

Hospital no:

Address:

Complaints:

Past History:

Diabetes mellitus

Hypertension

Ischemic Heart disease

Lung disease

Thyroid disease

Renal disease

Liver disease

Any other illness

Drug History:

Diuretics

Lipid lowering agents:

Steroids

Others

Personal History:

Diet

Smoking

Alcohol

Family History:

Cardiovascular disease

Hypertension

Hyperlipidemia:

Other

GENERAL PHYSICAL EXAMINATION:

Built

Height

Weight

BMI

Nutrition

Pallor

Icterus

Clubbing

Oedema

Cyanosis

Lymphadenopathy

Thyromegaly

VITALS:

BP (At 30 min interval) 1. 2. 3.

Pulse

Respiratory rate:

SYSTEMIC EXAMINATION:

1. Respiratory System

2. Cardiovascular System

3. Abdominal System

4. Nervous System

INVESTIGATIONS:

1. Serum Triglyceride mg/dl
2. Serum Cholesterol mg/dl
3. Serum VLDL mg/dl
4. Serum HDL mg/dl
5. Serum LDL mg/dl
6. Serum Uric acid mg/dl
7. Blood glucose mg/dl
8. Serum urea mg/dl
9. Serum creatinine mg/dl

ANNEXURE II – MASTER CHART

Group	S.NO	NAME	AGE	SEX	HEIGHT	WEIGHT	PULSE RATE/MIN	SBP	DBP	TRIGLYCERIDES	TOAL CHOLESTEROL	LDL	VLDL	HDL	SERUM URIC ACID	BLOOD GLUCOSE	SERUM UREA	CREATININE
HYPERTENSIVE	1	KOMBUDEVAR	58	MALE	170	68	72	172	110	272	257	155	54	48	8.9	120	20	0.8
HYPERTENSIVE	2	RAMACHANDRAN	36	MALE	172	66	74	144	100	138	180	110	28	42	6.9	130	18	0.7
HYPERTENSIVE	3	MURUGAN	46	MALE	172	59	73	156	100	176	206	129	35	42	7.9	110	24	0.9
HYPERTENSIVE	4	GANESAN	64	MALE	169	67	74	172	110	226	300	225	45	30	9	124	16	1
HYPERTENSIVE	5	GEORGE MATHEW	57	MALE	168	65	72	168	112	276	266	166	55	45	9.2	134	18	0.8
HYPERTENSIVE	6	SAMU	61	MALE	174	62	78	176	112	270	290	202	54	34	8.9	124	22	0.8
HYPERTENSIVE	7	MUTHUSAMY	52	MALE	173	68	72	162	100	257	275	168	51	56	7.6	114	24	0.8
HYPERTENSIVE	8	SAHID ALI	38	MALE	171	59	74	148	100	168	184	118	34	42	6.9	112	26	0.8
HYPERTENSIVE	9	JOHN ABRAHAM	58	MALE	168	65	76	178	100	294	281	184	59	38	9.6	124	18	0.7
HYPERTENSIVE	10	PAULRAJ	40	MALE	166	63	78	146	100	196	198	119	39	40	6.9	126	26	1
HYPERTENSIVE	11	ANTHONY	56	MALE	170	68	72	168	108	212	290	225	42	23	8.1	132	16	0.8
HYPERTENSIVE	12	ANNAMALAI	44	MALE	172	68	74	152	100	232	239	154	47	38	7.8	123	18	0.8
HYPERTENSIVE	13	MUBARAK ALI	63	MALE	169	66	72	170	100	241	293	214	48	31	8.4	102	24	0.8
HYPERTENSIVE	14	CHELLAIH	54	MALE	170	68	71	160	110	216	206	129	43	34	7.8	106	26	1
HYPERTENSIVE	15	SUDALAI	42	MALE	172	67	75	148	100	227	198	112	44	42	7.9	112	22	0.6
HYPERTENSIVE	16	GNANAM	46	FEMALE	165	58	76	152	100	232	244	164	46	34	7.8	118	24	0.8
HYPERTENSIVE	17	BHATHRAKALI	39	FEMALE	172	66	72	146	100	118	194	126	23	45	6.3	126	26	0.8
HYPERTENSIVE	18	GANDHIMATHI	48	FEMALE	160	64	74	162	104	212	232	155	42	35	7.6	130	24	0.9
HYPERTENSIVE	19	MULAKIAMMAL	51	FEMALE	168	55	76	166	100	265	255	168	53	34	7.9	124	28	0.7
HYPERTENSIVE	20	KALYANI	41	FEMALE	166	62	78	146	100	196	184	100	39	45	6.4	116	24	0.8
HYPERTENSIVE	21	ALAGARASI	54	FEMALE	164	61	71	158	100	208	278	205	41	32	7.8	106	18	0.9
HYPERTENSIVE	22	POKKODI	62	FEMALE	166	64	72	170	110	226	284	215	45	24	9.8	112	20	0.8
HYPERTENSIVE	23	GAJALAKHMI	58	FEMALE	162	59	74	168	108	268	252	162	54	36	8.6	108	22	0.8
HYPERTENSIVE	24	MUNIYAMAL	47	FEMALE	165	66	76	156	106	216	221	146	43	32	7.9	124	24	1
HYPERTENSIVE	25	LOGAMBAL	56	FEMALE	162	57	78	166	100	221	286	214	44	28	8.2	128	26	0.7
HYPERTENSIVE	26	VIJAYA	37	FEMALE	161	64	74	148	100	157	188	89	31	68	7.8	118	24	0.6
HYPERTENSIVE	27	NALLAMAI	59	FEMALE	158	72	72	170	100	210	316	244	42	30	9.2	114	22	0.8
HYPERTENSIVE	28	PARVATI	57	FEMALE	160	68	72	164	100	257	272	183	51	38	7.8	118	20	0.8
HYPERTENSIVE	29	RANI	53	FEMALE	162	59	71	164	106	223	297	226	44	27	7.8	110	18	0.8
HYPERTENSIVE	30	SENTHAMARAI	46	FEMALE	164	59	72	146	96	167	296	220	33	43	7.8	124	16	0.8
CONTROL	31	PALANIAPAN	38	MALE	170	68	72	124	80	110	152	62	22	68	5	120	22	0.8
CONTROL	32	SITTHIQ	48	MALE	168	65	74	120	80	108	136	50	22	64	5.2	130	20	0.6
CONTROL	33	ALAGU NAMBI	36	MALE	167	66	72	112	80	120	194	130	24	40	4.2	124	18	1
CONTROL	34	RAMA SUBBU	54	MALE	172	70	78	110	80	120	170	86	24	60	4.2	112	16	0.8
CONTROL	35	VASUDEVAN	58	MALE	165	64	74	130	80	122	142	76	24	42	4.6	126	24	0.7
CONTROL	36	KUPPUSAMY	64	MALE	164	62	72	130	80	224	158	70	46	42	5.6	106	28	0.9
CONTROL	37	MALAIAPPAN	44	MALE	169	65	74	120	80	124	194	119	25	50	5.2	112	16	0.8
CONTROL	38	MADHAYAN	46	MALE	172	68	76	110	80	106	160	95	21	44	4.6	108	22	1
CONTROL	39	VEERASAMY	61	MALE	170	68	72	120	80	110	214	128	22	54	5.2	124	18	0.8
CONTROL	40	ALEX MATHEW	56	MALE	168	67	74	110	80	126	164	79	25	60	4.8	126	28	0.8
CONTROL	41	SIRAJUDDIN	62	MALE	167	64	78	130	80	124	180	112	25	43	5.2	128	14	0.9
CONTROL	42	MANAVALAN	51	MALE	169	68	72	120	80	120	171	80	24	67	4.4	124	18	1
CONTROL	43	MOHAMMED ABDULLA	41	MALE	165	62	72	110	80	90	134	66	18	50	4.6	126	22	0.8
CONTROL	44	VETRIVEL	53	MALE	164	63	74	130	80	124	190	113	25	52	5.2	132	16	0.9
CONTROL	45	KANDASAMY	64	MALE	168	64	74	124	84	200	170	94	40	36	4.8	112	28	0
CONTROL	46	MARISELVAM	46	FEMALE	170	68	76	110	80	120	160	90	24	46	4.2	114	32	0.7
CONTROL	47	INDUMATHI	38	FEMALE	172	66	72	126	80	124	156	71	25	60	4.9	112	16	0.6
CONTROL	48	TAMILARASI	51	FEMALE	168	65	72	130	80	132	149	80	27	42	5.2	108	26	0.8
CONTROL	49	FATHIMA	42	FEMALE	165	62	74	120	80	142	154	72	28	54	5.6	118	14	1
CONTROL	50	UMAIYAMMAL	53	FEMALE	167	64	78	110	80	112	160	82	22	56	5.2	120	18	0.8
CONTROL	51	SAHMIMA BEGUM	44	FEMALE	168	62	72	120	80	130	152	74	26	52	4.8	124	22	0.8
CONTROL	52	VAIRAM	54	FEMALE	170	68	74	110	80	100	156	82	20	54	5.6	126	24	0.8
CONTROL	53	VIJAYA LAKSHMI	49	FEMALE	172	70	74	126	78	120	140	74	24	42	5.2	118	22	1
CONTROL	54	AJITHA	41	FEMALE	169	68	72	110	80	78	150	68	16	66	4.8	108	24	0.6
CONTROL	55	ESAKITHAI	62	FEMALE	168	64	74	120	80	210	168	80	42	42	4.8	104	18	0.6
CONTROL	56	VALLIAMMAL	51	FEMALE	165	64	76	130	80	124	140	73	25	42	5.6	114	28	0.8
CONTROL	57	ALEINA	39	FEMALE	172	68	78	120	82	78	180	110	16	54	5.4	126	24	1
CONTROL	58	CATHERINE	64	FEMALE	170	64	72	130	80	150	220	124	30	66	5.6	124	18	0.8
CONTROL	59	ARULARASI	47	FEMALE	168	67	74	120	80	80	198	132	16	50	4.8	124	16	0.9
CONTROL	60	ANBALAGI	56	FEMALE	167	66	72	120	80	220	190	104	44	42	5.6	126	22	0.8

ANNEXURE III

KEY TO MASTER CHART

Group

Hypertensive, control

Sex

Male, female

BMI

- Underweight < 18
- Normal – 18-24.9
- Grade I (over weight) -- 25-29.9
- Grade II (obese) – 30-39.9
- Grade III (very obese) > 40

BLOOD PRESSURE

HYPERTENSIVE - Systolic blood pressure >140mmhg,

Diastolic blood pressure >90mmhg

CONTROL - Systolic blood pressure <140mmhg,

Diastolic blood pressure <90mmhg

SERUM LIPID PROFILE – NORMAL VALUES

TRIGLYCERIDE - 30 to 200 MG/DL

TOTAL CHOLESTEROL - 150 to 200 MG/DL

LDL - 70 to130 MG/DL

HDL - 40 to 60 MG/DL

VLDL - 20 to 40 MG/DL

SERUM URIC ACID – NORMAL VALUES

MALE - 3.5 to 7 MG/DL

FEMALE - 2.7 to 6.5 MG/DL .

ANNEXURE – IV

LIST OF ABBREVIATIONS USED

BP – Blood Pressure

JNC- Joint National Committee

LDL- Low Density Lipoprotein

HDL- High Density Lipoprotein

VLDL- Very Low Density Lipoprotein

CCF- Congestive cardiac failure

HTN- Hypertension

CHD- Coronary Heart Disease

SBP- Systolic Blood Pressure

DBP- Diastolic Blood Pressure

ECF- Extra Cellular Fluid

ADH- Anti Diuretic Volume

ABM- Ambulatory Blood Pressure

WCH- White Coat Hypertension

LCAT- Lecithin Cholesterol Acyl Transferase

S.UA- Serum Uric Acid

STD- Standard

IDL- Intermediate Density lipoprotein

CNS-Central Nervous System

ICS- Inter Coastal Space

D/W- Distilled Water

BMI- Body Mass Index

OD- Optical Density

Conc.- Concentration.